

RESEARCH CENTER Nancy - Grand Est

FIELD

# Activity Report 2019

# **Section Application Domains**

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#### **ALICE Team**

# 4. Application Domains

#### 4.1. Geometric Tools for Simulating Physics with a Computer

Numerical simulation is the main targeted application domain for the geometry processing tools that we develop. Our mesh generation tools will be tested and evaluated within the context of our cooperation with Hutchinson, experts in vibration control, fluid management and sealing system technologies. We think that the hex-dominant meshes that we generate have geometrical properties that make them suitable for some finite element analyses, especially for simulations with large deformations.

We also have a tight collaboration with Wan Chiu Li, a geophysical modeling specialist. He is creating a start-up company MESHSPACE whose goal is to transfer to the industry remeshing tools we developed in the ALICE team. In particular, he uses hexahedral-dominant meshes for geomechanical simulations of gas and oil reservoirs. From a scientific point of view, this use case introduces new types of constraints (alignments with faults and horizons), and allows certain types of nonconformities that we did not consider until now.

Our cooperation with RhinoTerrain pursues the same goal: reconstruction of buildings from point cloud scans allows to perform 3D analysis and studies on insolation, floods and wave propagation, wind and noise simulations necessary for urban planification.

### **BIGS Project-Team**

# 4. Application Domains

#### 4.1. Tumor growth-oncology

On this topic, we want to propose branching processes to model appearance of mutations in tumor through new collaborations with clinicians. The observed process is the "circulating DNA" (ctDNA). The final purpose is to use ctDNA as a early biomarker of the resistance to an immunotherapy treatment. It is the aim of the ITMO project. Another topic is the identification of dynamic network of expression. In the ongoing work on low-grade gliomas, a local database of 400 patients will be soon available to construct models. We plan to extend it through national and international collaborations (Montpellier CHU, Montreal CRHUM). Our aim is to build a decision-aid tool for personalised medicine. In the same context, there is a topic of clustering analysis of a brain cartography obtained by sensorial simulations during awake surgery.

#### 4.2. Genomic data and micro-organisms population

Despite of his 'G' in the name of BIGS, Genetics is not central in the applications of the team. However, we want to contribute to a better understanding of the correlations between genes trough their expression data and of the genetic bases of drug response and disease. We have contributed to methods detecting proteomics and transcriptomics variables linked with the outcome of a treatment.

#### 4.3. Epidemiology and e-health

We have many works to do in our ongoing projects in the context of personalized medicine with CHU Nancy. They deal with biomarkers research, prognostic value of quantitative variables and events, scoring, and adverse events. We also want to develop our expertise in rupture detection in a project with APHP (Assistance Publique Hôpitaux de Paris) for the detection of adverse events, earlier than the clinical signs and symptoms. The clinical relevance of predictive analytics is obvious for high-risk patients such as those with solid organ transplantation or severe chronic respiratory disease for instance. The main challenge is the rupture detection in multivariate and heterogeneous signals (for instance daily measures of electrocardiogram, body temperature, spirometry parameters, sleep duration, etc. Other collaborations with clinicians concern foetopathology and we want to use our work on conditional distribution function to explain fetal and child growth. We have data from the "Service de foetopathologie et de placentologie" of the "Maternité Régionale Universitaire" (CHU Nancy).

#### **4.4. Dynamics of telomeres**

Telomeres are disposable buffers at the ends of chromosomes which are truncated during cell division; so that, over time, due to each cell division, the telomere ends become shorter. By this way, they are markers of aging. Trough a collaboration with Pr A. Benetos, geriatrician at CHU Nancy, we recently obtained data on the distribution of the length of telomeres from blood cells. With members of Inria team TOSCA, we want to work in three connected directions: (1) refine methodology for the analysis of the available data; (2) propose a dynamical model for the lengths of telomeres and study its mathematical properties (long term behavior, quasi-stationarity, etc.); and (3) use these properties to develop new statistical methods. A slot of postdoc position is already planned in the Lorraine Université d'Excellence, LUE project GEENAGE (managed by CHU Nancy).

### **CAMUS Project-Team**

# 4. Application Domains

### 4.1. Application Domains

Computational performance being our main objective, our target applications are characterized by intensive computation phases. Such applications are numerous in the domains of scientific computations, optimization, data mining and multimedia.

Applications involving intensive computations are necessarily high energy consumers. However this consumption can be significantly reduced thanks to optimization and parallelization. Although this issue is not our prior objective, we can expect some positive effects for the following reasons:

- Program parallelization tries to distribute the workload equally among the cores. Thus an equivalent performance, or even a better performance, to a sequential higher frequency execution on one single core, can be obtained.
- Memory and memory accesses are high energy consumers. Lowering the memory consumption, lowering the number of memory accesses and maximizing the number of accesses in the low levels of the memory hierarchy (registers, cache memories) have a positive consequence on execution speed, but also on energy consumption.

### **CAPSID Project-Team**

# 4. Application Domains

#### 4.1. Biomedical Knowledge Discovery

**Participants:** Marie-Dominique Devignes [contact person], Malika Smaïl-Tabbone [contact person], Sabeur Aridhi, David Ritchie, Gabin Personeni, Seyed Ziaeddin Alborzi, Kevin Dalleau, Bishnu Sarker, Emmanuel Bresso, Claire Lacomblez, Floriane Odje, Athénaïs Vaginay.

Our main application for Axis 1 : "New Approaches for Knowledge Discovery in Structural Databases", concerns biomedical knowledge discovery. We intend to develop KDD approaches on preclinical (experimental) or clinical datasets integrated with knowledge graphs with a focus on discovering which PPIs or molecular machines play an essentiel role in the onset of a disease and/or for personalized medicine.

As a first step we have been involved since 2015 in the ANR RHU "FIGHT-HF" (Fight Heart Failure) project, which is coordinated by the CIC-P (Centre d'Investigation Clinique Plurithématique) at the CHRU Nancy and INSERM U1116. In this project, the molecular mechanisms that underly heart failure (HF) are re-visited at the cellular and tissue levels in order to adapt treatments to patients' needs in a more personalized way. The Capsid team is in charge of a workpackage dedicated to network science. A platform has been constructed with the help of a company called Edgeleap (Utrecht, NL) in which biological molecular data and ontologies, available from public sources, are represented in a single integrated complex network also known as knowledge graph. We are developing querying and analysis facilities to help biologists and clinicians interpreting their cohort results in the light of existing interactions and knowledge. We are also currently analyzing pre-clinical data produced at the INSERM unit on the comparison of aging process in obese versus lean rats. Using our expertise in receptor-ligand docking, we are investigating possible cross-talks between mineralocorticoid and other nuclear receptors.

Another application is carried out in the context of a UL-funded interdisciplinary project in collaboration with the CRAN laboratory. It concerns the study of the role of estrogen receptors in the development of gliobastoma tumors. The available data is high-dimensional but involves rather small numbers of samples. The challenge is to identify relevant sets of genes which are differentially expressed in various phenoptyped groups (w.r.t. gender, age, tumor grade). The objectives are to infer pathways involving these genes and to propose candidate models of tumor development which will be experimentally tested thanks to an ex-vivo experimental system available at the CRAN.

Finally, simulating biological networks will be important to understand biological systems and test new hypotheses. One major challenge is the identification of perturbations responsible for the transformation of a healthy system to a pathological one and the discovery of therapeutic targets to reverse this transformation. Control theory, which consists in finding interventions on a system in order to prevent it to go in undesirable states or to force it to converge towards a desired state, is of great interest for this challenge. It can be formulated as "How to force a broken system (pathological) to act as it should do (normal state)?". Many formalisms are used to model biological processes, such as Differential Equations (DE), Boolean Networks (BN), cellular automata. In her PhD thesis, Athenaïs Vaginay investigates ways to find a BN fitting both the knowledge about topology and state transitions "inferred" from experimental data. This step is known as "boolean function synthesis". Our aim is to design automated methods for building biological networks and define operators to intervene on them[29]. Our approaches will be driven by knowledge and keep close connection with experimental data.

#### 4.2. Prokaryotic Type IV Secretion Systems

**Participants:** Marie-Dominique Devignes [contact person], Isaure Chauvot de Beauchêne [contact person], Bernard Maigret, David Ritchie, Philippe Noel, Antoine Moniot, Dominique Mias-Lucquin.

Concerning Axis 2 : "Integrative Multi-Component Assembly and Modeling", our first application domain is related to prokaryotic type IV secretion systems.

Prokaryotic type IV secretion systems constitute a fascinating example of a family of nanomachines capable of translocating DNA and protein molecules through the cell membrane from one cell to another [36]. The complete system involves at least 12 proteins. The structure of the core channel involving three of these proteins has recently been determined by cryo-EM experiments for Gram-negative bacteria [47], [63]. However, the detailed nature of the interactions between the other components and the core channel remains to be found. Therefore, these secretion systems represent a family of complex biological systems that call for integrated modeling approaches to fully understand their machinery.

In the framework of the Lorraine Université d'Excellence (LUE-FEDER) "CITRAM" project we are pursuing our collaboration with Nathalie Leblond of the Genome Dynamics and Microbial Adaptation (DynAMic) laboratory (UMR 1128, Université de Lorraine, INRA) on the mechanism of horizontal transfer by integrative conjugative elements (ICEs) and integrative mobilisable elements (IMEs) in prokaryotic genomes. These elements use Type IV secretion systems for transferring DNA horizontally from one cell to another. We have discovered more than 200 new ICEs/IMEs by systematic exploration of 72 Streptococcus genomes and characterized a new class of relaxases [21]. We have modeled the dimer of this relaxase protein by homology with a known structure. For this, we have created a new pipeline to model symmetrical dimers of multi-domains proteins. As one activity of the relaxase is to cut the DNA for its transfer, we are also currently studying the DNA-protein interactions that are involved in this very first step of horizontal transfer (see next section).

#### 4.3. Protein - Nucleic Acids Interactions

**Participants:** Isaure Chauvot de Beauchêne [contact person], David Ritchie, Dominique Mias-Lucquin, Antoine Moniot, Honey Jain, Anna Kravchenko, Hrishikesh Dhondge, Malika Smaïl-Tabbone, Marie-Dominique Devignes.

The second application domain of Axis 2 concerns protein-nucleic acids interactions. We need to assess and optimize our new algorithms on concrete protein-nucleic acids complexes in close collaboration with external partners coming from the experimental field of structural biology. To facilitate such collaborations, we will have to create automated and re-usable protein-nucleic acid docking pipelines.

This is the case for our PEPS collaboration "InterANRIL" with the IMoPA lab (CNRS-Université de Lorraine). We are currently working with biologists to apply our fragment-based docking approach to model complexes of the long non-coding RNA (lncRNA) ANRIL with proteins and DNA. In order to extend this approach to partially structured RNA molecules, we have built an automated pipeline to create (i) libraries of RNA fragments with arbitrary characteristics such as secondary structure, and (ii) testing benchmarks for applying these libraries to docking assays.

In the framework of our LUE-FEDER CITRAM project (see above), we adapted this approach and this pipeline to single-strand DNA docking in order to model the complex formed by a bacterial relaxase and its target DNA.

In the future, we will tackle a defined group of RNA-binding proteins containing RNA-Recognition Motif (RRM) domains. We will study existing and predicted complexes between various types of RRMs and various RNA sequences with computational methods in order to calculate CG force-field energy and to help design new synthetic proteins with targeted RNA specificity. This is the goal of the ITN RNAct project and it will require the construction of a dedicated database equipped with querying and analysis facilities, including machine-learning approaches, as well as many interactions within the ITN RNAct consortium.

### **CARAMBA Project-Team**

# 4. Application Domains

#### 4.1. Better Awareness and Avoidance of Cryptanalytic Threats

Our study of the Number Field Sieve family of algorithms aims at showing how the threats underlying various supposedly hard problems are real. Our record computations, as well as new algorithms, contribute to having a scientifically accurate assessment of the feasibility limit for these problems, given academic computing resources. The data we provide in this way is a primary ingredient for government agencies whose purpose includes guidance for the choice of appropriate cryptographic primitives. For example the French ANSSI <sup>0</sup>, German BSI, or the NIST <sup>0</sup> in the United States base their recommendations on such computational achievements.

The software we make available to achieve these cryptanalytic computations also allows us to give cost estimates for potential attacks to cryptographic systems that are taking the security/efficiency/legacy compatibility trade-offs too lightly. Attacks such as LogJam [26] are understood as being serious concerns thanks to our convincing proof-of-concepts. In the LogJam context, this impact has led to rapid worldwide security advisories and software updates that eventually defeat some potential intelligence threats and improve confidentiality of communications.

#### 4.2. Promotion of Better Cryptography

We also promote the switch to algebraic curves as cryptographic primitives. Those offer nice speed and excellent security, while primitives based on elementary number theory (integer factorization, discrete logarithm in finite fields), which underpin e.g., RSA, are gradually forced to adopt unwieldy key sizes so as to comply with the desired security guarantees of modern cryptography. Our contributions to the ultimate goal of having algebraic curves eventually take over the cryptographic landscape lie in our fast arithmetic contributions, our contributions to the point counting problem, and more generally our expertise on the diverse surrounding mathematical objects, or on the special cases where the discrete logarithm problem is not hard enough and should be avoided.

We also promote cryptographically sound electronic voting, for which we develop the Belenios prototype software (licensed under the AGPL). It depends on research made in collaboration with the PESTO team, and provides stronger guarantees than current state of the art.

#### **4.3. Key Software Tools**

The vast majority of our work is eventually realized as software. We can roughly categorize it in two groups. Some of our software covers truly fundamental objects, such as the GNU MPFR, GNU MPC, GF2X, or MPFQ packages. To their respective extent, these software packages are meant to be included or used in broader projects. For this reason, it is important that the license chosen for this software allows proper reuse, and we favor licenses such as the LGPL, which is not restrictive. We can measure the impact of this software by the way it is used in e.g., the GNU Compiler Collection (GCC), in Victor Shoup's Number Theory Library (NTL), or in the Sage computer algebra system. The availability of these software packages in most Linux distributions is also a good measure for the impact of our work.

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 $<sup>^{0}</sup>$ In [27], the minimal recommended RSA key size is 2048 bits for usage up to 2030. See also Annex B, in particular Section B.1 "Records de calculs cryptographiques".

<sup>&</sup>lt;sup>0</sup>The work [31] is one of only two academic works cited by NIST in the initial version (2011) of the report [33].

We also develop more specialized software. Our flagship software package is Cado-NFS [15], and we also develop some others with various levels of maturity, such as GMP-ECM, CMH, or Belenios, aiming at quite diverse targets. Within the lifespan of the CARAMBA project, we expect more software packages of this kind to be developed, specialized towards tasks relevant to our research targets: important mathematical structures attached to genus 2 curves, generation of cryptographically secure curves, or tools for attacking cryptographically hard problems. Such software both illustrates our algorithms, and provides a base on which further research work can be established. Because of the very nature of these specialized software packages as research topics in their own right, needing both to borrow material from other projects, and being possible source of inspiring material for others, it is again important that these be developed in a free and open-source development model.

#### **COAST Project-Team**

### 4. Application Domains

#### 4.1. Crisis Management

Crisis management research investigates all the dimensions regarding the management of unexpected catastrophic events like floods, earthquake or terrorist attacks. All the phases of a crisis, from preparedness to recovery require collaboration between people from many organizations. This provides opportunities to study inter-organizational collaboration at a large scale and to propose and evaluate mechanisms that ensure secure and safe collaboration. The work of Béatrice Linot provides us with a deep understanding of the factors that encourage collaboration and help to maintain trustworthy collaboration between stakeholders. This work is continued by Clélie Amiot who studies the effects of human chat-bot collaboration in this kind of setting.

#### 4.2. Collaborative Editing

Collaborative editing is a common application of optimistic replication in distributed settings. The goal of collaborative editors, irrespective of the kind of document, is to allow a group of users to update a document concurrently while ensuring that they eventually get all the same copy at the end. Our algorithm allows to implement collaborative editor in a peer to peer way. It avoids the need for a central server ensuring a higher level of privacy among collaborators. In this context, it requires to consider the problem of authentication and authorization of participants[4] and of trust between them[7].

#### **GAMBLE Project-Team**

# 4. Application Domains

#### 4.1. Applications of computational geometry

Many domains of science can benefit from the results developed by GAMBLE. Curves and surfaces are ubiquitous in all sciences to understand and interpret raw data as well as experimental results. Still, the nonlinear problems we address are rather basic and fundamental, and it is often difficult to predict the impact of solutions in that area. The short-term industrial impact is likely to be small because, on basic problems, industries have used ad hoc solutions for decades and have thus got used to it. The example of our work on quadric intersection is typical: even though we were fully convinced that intersecting 3D quadrics is such an elementary/fundamental problem that it ought to be useful, we were the first to be astonished by the scope of the applications of our software <sup>0</sup> (which was the first and still is the only one —to our knowledge– to compute robustly and efficiently the intersection of 3D quadrics) which has been used by researchers in, for instance, photochemistry, computer vision, statistics, and mathematics. Our work on certified drawing of plane (algebraic) curves falls in the same category. It seems obvious that it is widely useful to be able to draw curves correctly (recall also that part of the problem is to determine where to look in the plane) but it is quite hard to come up with specific examples of fields where this is relevant. A contrario, we know that certified meshing is critical in mechanical-design applications in robotics, which is a non-obvious application field. There, the singularities of a manipulator often have degrees higher than 10 and meshing the singular locus in a certified way is currently out of reach. As a result, researchers in robotics can only build physical prototypes for validating, or not, the approximate solutions given by non-certified numerical algorithms.

The fact that several of our pieces of software for computing non-Euclidean triangulations had already been requested by users long before they become public in CGAL is a good sign for their wide future impact. This will not come as a surprise, since most of the questions that we have been studying followed from discussions with researchers outside computer science and pure mathematics. Such researchers are either users of our algorithms and software, or we meet them in workshops. Let us only mention a few names here. Rien van de Weijgaert [55], [69] (astrophysicist, Groningen, NL) and Michael Schindler [66] (theoretical physicist, ENSPCI, CNRS, France) used our software for 3D periodic weighted triangulations. Stephen Hyde and Vanessa Robins (applied mathematics and physics at Australian National University) used our package for 3D periodic meshing. Olivier Faugeras (neuromathematics, Inria Sophia Antipolis) had come to us and mentioned his needs for good meshes of the Bolza surface [45] before we started to study them. Such contacts are very important both to get feedback about our research and to help us choose problems that are relevant for applications. These problems are at the same time challenging from the mathematical and algorithmic points of view. Note that our research and our software are generic, i.e., we are studying fundamental geometric questions, which do not depend on any specific application. This recipe has made the sucess of the CGAL library.

Probabilistic models for geometric data are widely used to model various situations ranging from cell phone distribution to quantum mechanics. The impact of our work on probabilistic distributions is twofold. On the one hand, our studies of properties of geometric objects built on such distributions will yield a better understanding of the above phenomena and has potential impact in many scientific domains. On the other hand, our work on simulations of probabilistic distributions will be used by other teams, more maths oriented, to study these distributions.

<sup>0</sup>QI: web.

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### **LARSEN Project-Team**

### 4. Application Domains

#### 4.1. Personal Assistance

During the last fifty years, many medical advances as well as the improvement of the quality of life have resulted in a longer life expectancy in industrial societies. The increase in the number of elderly people is a matter of public health because although elderly people can age in good health, old age also causes embrittlement, in particular on the physical plan which can result in a loss of autonomy. That will force us to re-think the current model regarding the care of elderly people. <sup>0</sup> Capacity limits in specialized institutes, along with the preference of elderly people to stay at home as long as possible, explain a growing need for specific services at home.

Ambient intelligence technologies and robotics could contribute to this societal challenge. The spectrum of possible actions in the field of elderly assistance is very large. We will focus on activity monitoring services, mobility or daily activity aids, medical rehabilitation, and social interactions. This will be based on the experimental infrastructure we have built in Nancy (Smart apartment platform) as well as the deep collaboration we have with OHS.<sup>0</sup>

#### 4.2. Civil Robotics

Many applications for robotics technology exist within the services provided by national and local government. Typical applications include civil infrastructure services <sup>0</sup> such as: urban maintenance and cleaning; civil security services; emergency services involved in disaster management including search and rescue; environmental services such as surveillance of rivers, air quality, and pollution. These applications may be carried out by a wide variety of robot and operating modality, ranging from single robots or small fleets of homogeneous or heterogeneous robots. Often robot teams will need to cooperate to span a large workspace, for example in urban rubbish collection, and operate in potentially hostile environments, for example in disaster management. These systems are also likely to have extensive interaction with people and their environments.

The skills required for civil robots match those developed in the LARSEN project: operating for a long time in potentially hostile environment, potentially with small fleets of robots, and potentially in interaction with people.

<sup>&</sup>lt;sup>0</sup>See the Robotics 2020 Multi-Annual Roadmap [35].

<sup>&</sup>lt;sup>0</sup>OHS (Office d'Hygiène Sociale) is an association managing several rehabilitation or retirement home structures.

<sup>&</sup>lt;sup>0</sup>See the Robotics 2020 Multi-Annual Roadmap [35], section 2.5.

#### **MAGRIT Team**

# 4. Application Domains

#### 4.1. Augmented reality

We have a significant experience in AR that allowed good progress in building usable, reliable and robust AR systems. Our contributions cover the entire process of AR: matching, pose initialization, 3D tracking, in-situ modeling, handling interaction between real and virtual objects....

#### 4.2. Medical Imaging

For 20 years, we have been working in close collaboration with University Hospital of Nancy and GE Healthcare in interventional neuroradiology. Our common aim is to develop a multimodality framework to assist therapeutic decisions and interventional gestures. Contributions of the team focus on the development of AR tools for neuro-navigation as well as the development of simulation tools for training or planning. Laparoscopic surgery is another field of interest with the development of methods for tracking deformable organs based on bio-mechanical models. Some of these projects are developed in collaboration with the MIMESIS project team.

#### **4.3.** Experimental mechanics

In experimental solid mechanics, an important problem is to characterize properties of specimens subject to mechanical constraints, which makes it necessary to measure tiny strains. Contactless measurement techniques have emerged in the last few years and are spreading quickly. They are mainly based on images of the surface of the specimen on which a regular grid or a random speckle has been deposited. We are engaged since June 2012 in a transdisciplinary collaboration with Institut Pascal (Clermont-Ferrand Université). The aim is to characterize the metrological performances of these techniques limited by, e.g., the sensor noise, and to improve them by several dedicated image processing tools.

#### **MFX Project-Team**

# 4. Application Domains

### 4.1. Digital Manufacturing

Our work addresses generic challenges related to fabrication and can thus be applied in a wide variety of contexts. Our aim is first and foremost to develop the algorithms that will allow various industrial sectors to benefit more strongly from the potential of AM. To enable this, we seek collaborations with key industry partners developing software and AM systems for a variety of processes and materials that are of interest to specific sectors (*e.g.*, dental, prosthetic, automotive, aerospace).

#### 4.2. Medical Applications

To allow for faster transfer of our techniques and unlock novel applications, we actively seek to develop applications in the medical sector. In particular, we are involved in a project around the design of orthoses which explores how our research on elasticity control through microstructure geometries can be specifically applied to the medical sector; see §9.1.1.

#### **MIMESIS Team**

# 4. Application Domains

#### 4.1. Surgical training

Virtual training helps medical students to get familiar with surgical procedures before manipulation of real patients. The development of simulation used for medical training usually requires important computational power, since realistic behaviors are key to deliver a high-fidelity experience to the trainee. Further, the quality of interaction with the simulator (usually via visual and haptic rendering) is also of paramount importance. All these constraints make the development of training systems time-consuming, thus limiting the deployment of virtual simulators in standard medical curriculum.

#### 4.2. Pre-operative planning

Beyond training, clinicians ask for innovative tools that can assist them in the pre-operative planning of an intervention. Using the patient information acquired before the operation, physics-based simulations allow to simulate the effect of therapy with no risk to the patient. The clinicians can thus virtually assess different strategies and select the optimal procedure. Compared to a training simulation, a planning system requires a high accuracy to ensure reliability. Constrained by the time elapsed between the preoperative acquisition and the intervention, the computation must also be efficient.

### 4.3. Intra-operative guidance

Besides the surgery training and planning, another major need from clinicians is surgical guidance. While the clinician is performing the operation, a guidance system provides enriched visual feedback. This is especially useful with the emergence of minimally invasive surgery (MIS) where the visual information is often strongly limited. It can be used for example to avoid critical areas such as vessels or to highlight the position of a tumor during its resection. In the MIS technique, the clinician does not interact with organs directly as in the open surgery, but manipulates instruments inserted through trocars placed in small incisions in the wall of the abdominal cavity. The surgeon can observe these instruments on a display showing a video stream captured by an endoscopic camera inserted through the navel. The main advantage of the method resides in reducing pain and time recovery, in addition to reducing bleeding and risks of infection. However, from a surgical standpoint, the procedure is quite complex since the field of view is considerably reduced and the direct manipulation of organs is not possible.

#### **MOCQUA Team**

# 4. Application Domains

#### **4.1. Quantum Computing**

Quantum Computing is currently the most promising technology to extend Moore's law, whose end is expected with the engraving at 7 nm, in less than 5 years. Thanks to the exponential computational power it will bring, it will represent a decisive competitive advantage for those who will control it.

Quantum Computing is also a major security issue, since it allows us to break today's asymmetric cryptography. Hence, mastering quantum computing is also of the highest importance for national security concerns. Recent scientific and technical advances suggest that the construction of the first quantum computers will be possible in the coming years.

As a result, the major US players in the IT industry have embarked on a dramatic race, mobilizing huge resources: IBM, Microsoft, Google and Intel have each invested between 20 and 50 million euros, and are devoting significant budgets to attract and hire the best scientists on the planet. Some states have launched ambitious national programs, including Great Britain, the Netherlands, Canada, China, Australia, Singapore, and very recently Europe, with the upcoming 10-year FET Flagship program in Quantum Engineering.

While a large part of these resources are going towards R-&-D in quantum hardware, there is still an important need and real opportunities for leadership in the field of quantum software.

The Mocqua team contributes to the computer science approach to quantum computing, aka the quantum software approach. We aim at a better understanding of the power and limitations of the quantum computer, and therefore of its impact on society. We also contribute to ease the development of the quantum computer by filling the gap between the theoretical results on quantum algorithms and complexity and the recent progresses in quantum hardware.

#### 4.2. Higher-Order Computing

The idea of considering functions as first-class citizens and allowing programs to take functions as inputs has emerged since the very beginning of theoretical computer science through Church's  $\lambda$ -calculus and is nowadays at the core of functional programming, a paradigm that is used in modern software and by digital companies (Google, Facebook, ...). In the meantime higher-order computing has been explored in many ways in the fields of logic and semantics of programming languages.

One of the central problems is to design programming languages that capture most of, if not all, the possible ways of computing with functions as inputs. There is no Church thesis in higher-order computing and many ways of taking a function as input can be considered: allowing parallel or only sequential computations, querying the input as a black-box or via an interactive dialog, and so on.

The Kleene-Kreisel computable functionals are arguably the broadest class of higher-order continuous functionals that could be computed by a machine. However their complexity is such that no current programming language can capture all of them. Better understanding this class of functions is therefore fundamental in order to identify the features that a programming language should implement to make the full power of higher-order computation expressible in such a language.

#### 4.3. Simulation of Dynamical Systems by Cellular Automata

We aim at developing various tools to simulate and analyse the dynamics of spatially-extended discrete dynamical systems such as cellular automata. The emphasis of our approach is on the evaluation of the robustness of the models under study, that is, their capacity to resist various perturbations.

In the framework of pure computational questions, various examples of such systems have already been proposed for solving complex problems with a simple bio-inspired approach (e.g. the decentralized gathering problem [40]). We are now working on their transposition to various real-world situations. For example when one needs to understand the behaviour of large-scale networks of connected components such as wireless sensor networks. In this direction of research, a first work has been presented on how to achieve a decentralized diagnosis of networks made of simple interacting components and the results are rather encouraging [5]. Nevertheless, there are various points that remain to be studied in order to complete this model for its integration in a real network.

We have also tackled the question of the evaluation of the robustness of a swarming model proposed by A. Deutsch to mimic the self-organization process observed in various natural systems (birds, fishes, bacteria, etc.) [2]. We now wish to develop our simulation tools to apply them to various biological phenomena where a great number of agents are implied.

We are also currently extending the range of applications of these techniques to the field of economy. We have started a collaboration with Massimo Amato, a professor in economy at the Bocconi University in Milan. Our aim is to examine how to propose a decentralized view of a business-to-business market and propose agent-oriented and totally decentralized models of such markets. Various banks and large businesses have already expressed their interest in such modelling approaches.

#### **MULTISPEECH Project-Team**

### 4. Application Domains

#### 4.1. Introduction

Approaches and models developed in the MULTISPEECH project are intended to be used for facilitating oral communication in various situations through enhancements of communication channels, either directly via automatic speech recognition or speech production technologies, or indirectly, thanks to computer assisted language learning. Applications also include the usage of speech technologies for helping people in handicapped situations or for improving their autonomy. Foreseen application domains are related to multimodal computer interaction, annotation and processing of spoken documents, health and autonomy (more precisely aided communication and monitoring), and computer assisted learning.

#### 4.2. Multimodal Computer Interactions

Speech synthesis has tremendous applications in facilitating communication in a human-machine interaction context to make machines more accessible. For example, it started to be widely common to use acoustic speech synthesis in smartphones to make possible the uttering of all the information. This is valuable in particular in the case of handicap, as for blind people. Audiovisual speech synthesis, when used in an application such as a talking head, i.e., virtual 3D animated face synchronized with acoustic speech, is beneficial in particular for hard-of-hearing individuals. This requires an audiovisual synthesis that is intelligible, both acoustically and visually. A talking head could be an intermediate between two persons communicating remotely when their video information is not available, and can also be used in language learning applications as vocabulary tutoring or pronunciation training tool. Expressive acoustic synthesis is of interest for the reading of a story, such as an audiobook, as well as for better human-machine interactions.

#### 4.3. Annotation and Processing of Spoken Documents and Audio Archives

A first type of annotation consists in transcribing a spoken document in order to get the corresponding sequences of words, with possibly some complementary information, such as the structure (punctuation) or the modality (affirmation/question) of the utterances to make the reading and understanding easier. Typical applications of the automatic transcription of radio or TV shows, or of any other spoken document, include making possible their access by deaf people, as well as by text-based indexing tools.

A second type of annotation is related to speech-text alignment, which aims at determining the starting and ending times of the words, and possibly of the sounds (phonemes). This is of interest in several cases such as for annotating speech corpora for linguistic studies, and for synchronizing lip movements with speech sounds (for example, for avatar-based communications). Although good results are currently achieved on clean data, automatic speech-text alignment needs to be improved for properly processing noisy spontaneous speech data and needs to be extended to handle overlapping speech.

Finally, there is also a need for speech signal processing techniques in the field of multimedia content creation and rendering. Relevant techniques include speech and music separation, speech equalization, speech enhancement, prosody modification, and speaker conversion.

#### 4.4. Aided Communication and Monitoring

Source separation techniques should help for locating and monitoring people through the detection of sound events inside apartments, and speech enhancement is mandatory for hands-free vocal interactions. A foreseen application aims at improving the autonomy of elderly or disabled people, and also fits with smartroom applications. In a longer perspective, adapting speech recognition technologies to the voice of elderly people should also be useful for such applications, but this requires the recording of adequate databases. Sound monitoring in other application fields (security, environmental monitoring) can also be envisaged.

#### 4.5. Computer Assisted Learning

Although speaking seems quite natural, learning foreign languages, or learning the mother tongue for people with language deficiencies, represents critical cognitive stages. Hence, many scientific activities have been devoted to these issues either from a production or a perception point of view. The general guiding principle with respect to computer assisted mother or foreign language learning is to combine modalities or to augment speech to make learning easier. Based upon an analysis of the learner's production, automatic diagnoses can be considered. However, making a reliable diagnosis on each individual utterance is still a challenge, which is dependent on the precision and quality of the segmentation of the speech utterance into phones, and of the computed prosodic parameters.

### **NEUROSYS Project-Team**

# 4. Application Domains

#### 4.1. Medical applications

Our research directions are motivated by applications with a high healthcare or social impact. They are developed in collaboration with medical partners, neuroscientists and psychologists. Almost all of our applications can be seen as neural interfaces which require the analysis and modeling of sensorimotor rhythms.

#### 4.1.1. Per-operative awareness during general anesthesia

*Collaborators*: Univ. Hospital of Nancy-Brabois/dept. Anesthesia & Resuscitation During general anesthesia, brain oscillations change according to the anesthetic drug concentration. Nowadays, 0.2 to 1.3% of patients regain consciousness during surgery and suffer from post-traumatic disorders. Despite the absence of subject movements due to curare, an electroencephalographic analysis of sensorimotor rhythms can help to detect an intention of movement. Within a clinical protocol, we are working on a

brain-computer interface adapted to the detection of intraoperative awareness.

#### 4.1.2. Recovery after stroke

*Collaborators*: Regional Institute of Physical Medicine and Rehabilitation/Center for Physical Medicine and Rehabilitation (Lay St Christophe), Univ. of Lorraine/PErSEUs.

Stroke is the main cause of acquired disability in adults. Neurosys aims at recovering limb control by improving the kinesthetic motor imagery (KMI) generation of post-stroke patients. We propose to design a KMI-based EEG neural interface which integrates complementary modalities of interactions such as tangible and haptic ones to stimulate the sensorimotor loop. This solution would provide a more engaging and compelling stroke rehabilitation training program based on KMI production.

#### 4.1.3. Modeling Parkinson's disease

*Collaborators*: Center for Systems Biomedicine (Luxembourg), Institute of Neurodegenerative Diseases (Bordeaux), Human Performance & Robotics laboratory (California State Univ., Long Beach).

Effective treatment of Parkinson's disease should be based on a realistic model of the disease. We are currently developing a neuronal model based on Hodgkin-Huxley neurons reproducing to a certain extent the pathological synchronization observed in basal ganglia in Parkinsonian rats. Moreover, our mesoscopic models of plastic Central Pattern Generator neural circuitries involved in rhythmic movements will allow us to reproduce incoherent coordination of limbs observed on humans affected by Parkinson's diseases like frozen gait, crouch gait. Our long-term objective is to understand how oscillatory activity in the basal ganglia affects motor control in spinal structures.

#### 4.1.4. Modeling propagation of epileptic spikes

*Collaborators*: Epileptology Unit of the CHRU Nancy (University hospital), CRAN (Research Center in Automation and Signal Processing of Nancy). Effective treatment of patients with refractory epilepsy requires a better understanding of the underlying neuronal mechanisms. In particular, it has been observed that epileptic spikes propagate more easily during stage III sleep (slow wave sleep) than during wakefulness, but the origin of these behaviours still remains misunderstood. At least both, a combination of anatomical structure/connectivity changes and changes in level of neurotransmitters, namely functional connectivity, can cause the propagation. A better knowledge of the functional and structural circuitry could allow a better targetting of structures to be treated, either surgically or pharmacologically, and to better individually adapt the pharmacology to each patient according to their symptomatology.

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### **ORPAILLEUR Project-Team**

# 4. Application Domains

#### 4.1. Life Sciences: Agronomy, Biology, Chemistry, and Medicine

**Keywords:** knowledge discovery in life sciences, biology, chemistry, medicine, pharmacogenomics and precision medicine.

One major application domain which is currently investigated by the Orpailleur team is related to life sciences, with particular emphasis on biology, medicine, and chemistry. The understanding of biological systems provides complex problems for computer scientists, and the developed solutions bring new research ideas or possibilities for biologists and for computer scientists as well. Indeed, the interactions between researchers in biology and researchers in computer science improve not only knowledge about systems in biology, chemistry, and medicine, but knowledge about computer science as well.

Knowledge discovery is gaining more and more interest and importance in life sciences for mining either homogeneous databases such as protein sequences and structures, or heterogeneous databases for discovering interactions between genes and the environment, or between genetic and phenotypic data, especially for public health and precision medicine (pharmacogenomics). Pharmacogenomics is one main challenge for the Orpailleur team as it considers a large panel of complex data ranging from biological to medical data, and various kinds of encoded domain knowledge ranging from texts to formal ontologies.

On the same line as biological data, chemical data are presenting important challenges w.r.t. knowledge discovery, for example for mining collections of molecular structures and collections of chemical reactions in organic chemistry. The mining of such collections is an important task for various reasons including the challenge of graph mining and the industrial needs (especially in drug design, pharmacology and toxicology). Molecules and chemical reactions are complex data that can be modeled as labeled graphs. Graph mining and Formal Concept Analysis methods play an important role in this application domain and can be used in an efficient and well-founded way [87].

Finally, research in agronomy is mainly based on cooperation between Inria and INRA. One research dimension is related to the characterization and the simulation of hedgerow structures in agricultural landscapes, based on Hilbert-Peano curves and Markov models [79]. Another research dimension is based on the mining of survey data for evaluating groundwater quality risks [86].

### **PESTO Project-Team**

# 4. Application Domains

#### 4.1. Cryptographic protocols

Security protocols, such as TLS, Kerberos, ssh or AKA (mobile communication), are the main tool for securing our communications. The aim of our work is to improve their security guarantees. For this, we propose models that are expressive enough to formally represent protocol executions in the presence of an adversary, formal definitions of the security properties to be satisfied by these protocols, and automated tools able to analyse them and possibly exhibit design flaws.

#### 4.2. Automated reasoning

Many techniques for symbolic verification of security are rooted in automated reasoning. A typical example is equational reasoning used to model the algebraic properties of a cryptographic primitive. Our work therefore aims to improve and adapt existing techniques or propose new ones when needed for reasoning about security.

#### 4.3. Electronic voting

Electronic elections have in the last years been used in several countries for politically binding elections. The use in professional elections is even more widespread. The aim of our work is to increase our understanding of the security properties needed for secure elections, propose techniques for analysing e-voting protocols, design of state-of-the-art voting protocols, but also to highlight the limitations of e-voting solutions.

#### 4.4. Privacy in social networks

The treatment of information released by users on social networks can violate a user's privacy. The goal of our work is to allow users to control the information released while guaranteeing their privacy.

#### **RESIST Team**

# 4. Application Domains

#### 4.1. Internet

Among the different network types, the Internet is the one to link them all and is consequently our most prominent subject, not to mention its prime importance in today's society. The Internet also exhibits its own challenges due to the scale and diversity of stakeholders, applications and network technologies in use.

From a security perspective, **monitoring and analysing Internet traffic is an important part of threat prevention and predictive security**. Indeed, large network telescopes like the one we use in the High Security Laboratory<sup>0</sup> allow detecting world-wide campaigns of attacks which target a specific exploit in some applications. Moreover the monitoring of the Internet traffic at the **edge** is the best way to quickly detect distributed attacks like DDoS and to mitigate them before they become effective. However, the Internet traffic analysis is made much more complicated since the **massive shift towards encryption** that happened few years ago, which requires new traffic classification methods.

The performance and resilience of services running over the Internet is also a major topic of Resist. In particular, it is very difficult to **diagnose the cause of a degradation of performance among the different actors and technologies** that are used to deliver a service over the Internet (access medium, ISP, CDN, web-browser, etc.). Networked systems deployed at Internet scale are also a natural research subject for Resist. Indeed **decentralized systems** like P2P networks or blockchains are known to be robust and scalable. However, their security and performance have to be carefully assessed because a single flaw in their design can endanger the whole system.

#### 4.2. SDN and Data-Center Networks

As the SDN paradigm and its implementations bring new opportunities that can be leveraged in different contexts, in particular for security and performance, programmable networks are also part of the research scope of Resist. This includes data-plane **programming models and hardware offloading** that enable very flexible programming at the network level. While OpenFlow was initially designed for academic research, SDN in general has then been adopted by industrial players, above all in **data-center networks**. It supports innovations to better share load and optimize resources among processes, in particular for virtualization platforms. Contributing to the development of these technologies is primordial for us as they are key elements for monitoring and enhancing the performance and security of future data-center networks.

When defining or extending SDN technologies, the strongest constraint is to guarantee a satisfactory level of performance, i.e. enabling high flexibility in programming with a **reduced footprint of network throughput**. However, as it may also break isolation principles between multiple tenants, security has to carefully considered, either by adding safeguard mechanisms at run-time or through a priori verification and testing.

#### 4.3. Fog and Cloud computing

Cloud computing has largely evolved in the last years including new networking capabilities as highlighted in the previous section towards the model of XaaS or **everything-as-a-service**. Moreover, cloud computing continues to be more distributed and aims at integrating more heterogeneous resources. One particular example is **fog computing** that consists of a massively distributed number of different resources, including lowperformance ones. Large network operators have a great interest in fog computing because they already operate such an infrastructure (e.g. a national operator with regional clouds and setup boxes in end users' homes). Softwarization or virtualization of all functions and services will help them to be competitive by reducing their costs. In general, intelligent orchestration of massively distributed resources will be investigated in various application domains, including **federated cloud infrastructures**, **fog computing**, **5G networks**, **IoT and big data infrastructures**.

<sup>&</sup>lt;sup>0</sup>https://lhs.loria.fr

The manageability of such largely distributed systems is a core topic with questions related to monitoring, security and orchestration of resources. Major changes and errors can have dramatic effects on a real system, that actually lead to only minor changes being carried out and slow down innovation and adoption of new propositions. Hence, **controlled and reproducible experiments are vital**.

As shown by our past work, we are able to quickly adjust to experimental needs in most areas of distributed computing and networking, such as *High Performance Computing (HPC)*, *Big Data, Peer-to-peer systems, Grid computing*, etc. However, in the context of Resist, we will focus mainly on *Software-Defined Infrastructures*, gathering *cloud computing* for compute and storage resources, *software-defined networking* and *network function virtualization* for networking. Those infrastructures share many common features: need for performance, for scalability, for resilience, all implemented using flexible software components.

Worth mentioning here is our involvement in the international testbed community (FIRE, GENI). We plan to strengthen our existing links with the Chameleon and CloudLab US projects, to leverage the recently accepted Fed4FIRE+ project on a testbed federation, and, at the national level, to contribute to the SILECS initiative for a new large-scale experimental computer science infrastructure.

### 4.4. Cyber-Physical Systems

Cyber-Physical Systems (CPSs) used to be well isolated and so designed accordingly. In the last decade, they have become **integrated within larger systems** and so accessible through the Internet. This is the case with **industrial systems**, like SCADA, that have been unfortunately exposed to major threats. Furthermore, the **Internet-of-Things (IoT)** has become a reality with numerous protocols, platforms and devices being developed and used to support the growing deployment of smart\* services: smart home, transport, health, city... and even rather usual rigid systems such as industry 4.0.

From an academic perspective, the IoT can be seen as an evolution of sensor networks. It thus inherits from the same problems regarding security and scalability, but with a higher order of magnitude both in terms of number of devices and their capabilities, which can be exploited by attackers. Research in this area has focused on developing dedicated protocols or operating systems to guarentee security and performance, Resist aims to tackle identical problems but **assuming a more practical deployment of IoT systems composed of heterogeneous and uncontrolled devices**. Indeed, this ecosystem is very rich and **cannot be controlled by a unique entity**, e.g. services are often developed by third parties, manufacturers of embed devices are different from those providing connectivity.

As a result, managing an IoT system (monitoring, changing configuration, etc.) is very hard to achieve as most of the devices or applications cannot be directly controlled. For instance, many IoT providers rely on their own cloud services, with their own unknown **proprietary protocols** and most of the time through **encrypted channels**. Above all, the use of middle-boxes like gateways hides the IoT end-devices and applications. We will thus need to infer knowledge from **indirect and partial observations**. Likewise, control will be also indirect for example through filtering or altering communications.

### **SEMAGRAMME Project-Team**

# 4. Application Domains

#### 4.1. Deep Semantic Analysis

Our applicative domains concern natural language processing applications that rely on a deep semantic analysis. For instance, one may cite the following ones:

- textual entailment and inference,
- dialogue systems,
- semantic-oriented query systems,
- content analysis of unstructured documents,
- text transformation and automatic summarization,
- (semi) automatic knowledge acquisition.

### 4.2. Text Transformation

Text transformation is an application domain featuring two important sub-fields of computational linguistics:

- parsing, from surface form to abstract representation,
- generation, from abstract representation to surface form.

Text simplification or automatic summarization belong to that domain.

We aim at using the framework of Abstract Categorial Grammars we develop to this end. It is indeed a reversible framework that allows both parsing and generation. Its underlying mathematical structure of  $\lambda$ -calculus makes it fit with our type-theoretic approach to discourse dynamics modeling.

### **SPHINX Project-Team**

# 4. Application Domains

#### 4.1. Robotic swimmers

Some companies aim at building biomimetic robots that can swim in an aquarium, as toys but also for medical purposes. An objective of Sphinx is to model and to analyze several models of these robotic swimmers. For the moment, we focus in the motion of a nanorobot. In that case, the size of the swimmers leads to neglect the inertia forces and to only consider the viscosity effects. Such nanorobots could be used for medical purposes to introduce some medicine or perform small surgical operations. In order to get a better understanding of such robotic swimmers, we have obtained control results via shape changes and we have developed simulation tools (see [71], [70], [101], [98]). Among all the important issues, we aim to consider the following ones:

- 1. Solve the control problem by limiting the set of admissible deformations.
- 2. Find the "best" location of the actuators, in the sense of being the closest to the exact optimal control.

The main tools for this investigation are the 3D codes that we have developed for simulation of fish in a viscous incompressible fluid (SUSHI3D) or in a inviscid incompressible fluid (SOLEIL).

#### 4.2. Aeronautics

We will develop robust and efficient solvers for problems arising in aeronautics (or aerospace) like electromagnetic compatibility and acoustic problems related to noise reduction in an aircraft. Our interest for these issues is motivated by our close contacts with companies like Airbus or "Thales Systèmes Aéroportés". We will propose new applications needed by these partners and assist them in integrating these new scientific developments in their home-made solvers. In particular, in collaboration with C. Geuzaine (Université de Liège), we are building a freely available parallel solver based on Domain Decomposition Methods that can handle complex engineering simulations, in terms of geometry, discretization methods as well as physics problems, see http://onelab.info/wiki/GetDDM.

#### **TONUS Project-Team**

### 4. Application Domains

#### 4.1. Controlled fusion and ITER

The search for alternative energy sources is a major issue for the future. Among others, controlled thermonuclear fusion in a hot hydrogen plasma is a promising possibility. The principle is to confine the plasma in a toroidal chamber, called a tokamak, and to attain the necessary temperatures to sustain nuclear fusion reactions. The International Thermonuclear Experimental Reactor (ITER) is a tokamak being constructed in Cadarache, France. This was the result of a joint decision by an international consortium including the European Union, Canada, USA, Japan, Russia, South Korea, India and China. ITER is a huge project. As of today, the budget is estimated at 20 billion euros. The first plasma shot is planned for 2020 and the first deuterium-tritium operation for 2027. Many technical and conceptual difficulties have to be overcome before the actual exploitation of fusion energy. Consequently, much research has been carried out around magnetically confined fusion. Among these studies, it is important to carry out computer simulations of the burning plasma. Thus, mathematicians and computer scientists are also needed in the design of ITER. The reliability and the precision of numerical simulations allow a better understanding of the physical phenomena and thus would lead to better designs. TONUS's main involvement is in such research. The required temperatures to attain fusion are very high, of the order of a hundred million degrees. Thus it is imperative to prevent the plasma from touching the tokamak inner walls. This confinement is obtained thanks to intense magnetic fields. The magnetic field is created by poloidal coils, which generate the toroidal component of the field. The toroidal plasma current also induces a poloidal component of the magnetic field that twists the magnetic field lines. The twisting is very important or the stability of the plasma. The idea goes back to research by Tamm and Sakharov, two Russian physicists, in the 50's. Other devices are essential for the proper operation of the tokamak: divertor for collecting the escaping particles, microwave heating for reaching higher temperatures, fuel injector for sustaining the fusionr eactions, toroidal coils for controlling instabilities, etc.

#### 4.2. Other applications

The software and numerical methods that we develop can also be applied to other fields of physics or of engineering.

- For instance, we have a collaboration with the company AxesSim in Strasbourg for the development of efficient Discontinuous Galerkin (DG) solvers on hybrid computers (CPU/GPU). The applications are electro-magnetic simulations for the conception of antennas, electronic devices or aircraft electromagnetic compatibility.
- The acoustic conception of large rooms requires huge numerical simulations. It is not always possible to solve the full wave equation and many reduced acoustic models have been developed. A popular model consists in considering "acoustic" particles moving at the speed of sound. The resulting Partial Differential Equation (PDE) is very similar to the Vlasov equation. The same modelling is used in radiation theory. We have started to work on the reduction of the acoustic particles model and realized that our reduction approach perfectly applies to this situation. A PhD with CEREMA (Centre d'études et d'expertise sur les risques, l'environnement, la mobilité et l'aménagement) has started in October 2015 (PhD of Pierre Gerhard). The objective is to investigate the model reduction and to implement the resulting acoustic model in our DG solver.
- In September 2017, we started a collaboration with EDF Chatou (PhD of Lucie Quibel) on the modelling of multiphase fluids with complex equations of state. The goal is to simulate the high temperature liquid-vapor flow occurring in a nuclear plant. Among others, we will apply our recent kinetic method for designing efficient implicit schemes for this kind of flows.

### **TOSCA Team**

# 4. Application Domains

#### 4.1. Application domains

TOSCA is interested in developing stochastic models and probabilistic numerical methods. Our present motivations come from models with singular coefficients, with applications in Geophysics, Molecular Dynamics and Neurosciences; Lagrangian modeling in Fluid Dynamics and Meteorology; Population Dynamics, Evolution and Genetics; Neurosciences; and Financial Mathematics.

#### 4.1.1. Stochastic models with singular coefficients: Analysis and simulation

Stochastic differential equations with discontinuous coefficients arise in Geophysics, Chemistry, Molecular Dynamics, Neurosciences, Oceanography, etc. In particular, they model changes of diffusion of fluids, or diffractions of particles, along interfaces.

For practioners in these fields, Monte Carlo methods are popular as they are easy to interpret — one follows particles — and are in general easy to set up. However, dealing with discontinuities presents many numerical and theoretical challenges. Despite its important applications, ranging from brain imaging to reservoir simulation, very few teams in mathematics worldwide are currently working in this area. The Tosca project-team has tackled related problems for several years providing rigorous approach. Based on stochastic analysis as well as interacting with researchers in other fields, we developed new theoretical and numerical approaches for extreme cases such as Markov processes whose generators are of divergence form with discontinuous diffusion coefficient.

The numerical approximation of singular stochastic processes can be combined with backward stochastic differential equations (BSDEs) or branching diffusions to obtain Monte Carlo methods for quasi-linear PDEs with discontinuous coefficients. The theory of BSDEs has been extensively developed since the 1980s, but the general assumptions for their existence can be quite restrictive. Although the probabilistic interpretation of quasi-linear PDEs with branching diffusions has been known for a long time, there have been only a few works on the related numerical methods.

Another motivation to consider stochastic dynamics in a discontinuous setting came to us from time evolution of fragmentation and coagulation phenomena, with the objective to elaborate stochastic models for the avalanche formation of soils, snow, granular materials or other geomaterials. Most of the models and numerical methods for avalanches are deterministic and involve a wide variety of physical parameters such as the density of the snow, the yield, the friction coefficient, the pressure, the basal topography, etc. One of these methods consists in studying the safety factor (or limit load) problem, related to the shallow flow of a visco-plastic fluid/solid with heterogeneous thickness over complex basal topography. The resulting nonlinear partial differential equation of this last theory involves many singularities, which motivates us to develop an alternative stochastic approach based on our past works on coagulation and fragmentation. Our approach consists in studying the evolution of the size of a typical particle in a particle system which fragments in time.

#### 4.1.2. Stochastic Lagrangian modeling in Computational Fluid Dynamics

Stochastic Lagrangian models were introduced in the eighties to simulate complex turbulent flows, particularly two-phase flows. In Computational Fluid Dynamics (CFD), they are intensively used in the so-called Probability Density Functions (PDF) methods in order to model and compute the reaction-phase terms in the fundamental equations of fluid motions. The PDF methods are currently developed in various laboratories by specialists in scientific computation and physicists. However, to our knowledge, we are innovating in two ways:

- our theoretical studies are the pioneering mathematical analysis of Lagrangian stochastic models in CFD;
- our work on the Stochastic Downscaling Method (SDM) for wind simulation is the first attempt to solve the fundamental equations themselves by a fully 3D stochastic particle method.

We emphasize that our numerical analysis is essential to the SDM development which takes benefits from our deep expertise on numerical schemes for McKean-Vlasov-non-linear SDEs.

#### 4.1.3. Population Dynamics, Evolution and Genetics

The activity of the team on stochastic modeling in population dynamics and genetics mainly concerns application in adaptive dynamics, a branch of evolutionary biology studying the interplay between ecology and evolution, ecological modeling, population genetics in growing populations, and stochastic control of population dynamics, with applications to cancer growth modeling. Stochastic modeling in these areas mainly considers individual-based models, where the birth and death of each individual is described. This class of model is well-developed in Biology, but their mathematical analysis is still fragmentary. Another important topic in population dynamics is the study of populations conditioned to non-extinction, and of the corresponding stationary distributions, called quasi-stationary distributions (QSD). This domain has been the object of a lot of studies since the 1960's, but we made recently significant progresses on the questions of existence, convergence and numerical approximation of QSDs using probabilistic tools rather than the usual spectral tools.

Our activity in population dynamics also involves a fully new research project on cancer modeling at the cellular level by means of branching processes. In 2010 the International Society for Protons Dynamics in Cancer was launched in order to create a critical mass of scientists engaged in research activities on Proton Dynamics in Cancer, leading to the facilitation of international collaboration and translation of research to clinical development. Actually, a new branch of research on cancer evolution is developing intensively; it aims in particular to understand the role of proteins acting on cancerous cells' acidity, their effects on glycolysis and hypoxia, and the benefits one can expect from controlling pH regulators in view of proposing new therapies.

#### 4.1.4. Stochastic modeling in Neuroscience

It is generally accepted that many different neural processes that take place in the brain involve noise. Indeed, one typically observes experimentally underlying variability in the spiking times of an individual neuron in response to an unchanging stimulus, while a predictable overall picture emerges if one instead looks at the average spiking time over a whole group of neurons. Sources of noise that are of interest include ionic currents crossing the neural membrane, synaptic noise, and the global effect of the external environment (such as other parts of the brain).

It is likely that these stochastic components play an important role in the function of both the neurons and the networks they form. The characterization of the noise in the brain, its consequences at a functional level and its role at both a microscopic (individual neuron) level and macroscopic level (network of thousands of neurons) is therefore an important step towards understanding the nervous system.

To this end, a large amount of current research in the neuroscientific literature has involved the addition of noise to classical purely deterministic equations resulting in new phenomena being observed. The aim of the project is thus to rigorously study these new equations in order to be able to shed more light on the systems they describe.

#### 4.1.5. Stochastic modeling in Financial Mathematics

#### 4.1.5.1. Technical Analysis

In the financial industry, there are three main approaches to investment: the fundamental approach, where strategies are based on fundamental economic principles; the technical analysis approach, where strategies are based on past price behavior; and the mathematical approach where strategies are based on mathematical models and studies. The main advantage of technical analysis is that it avoids model specification, and thus calibration problems, misspecification risks, etc. On the other hand, technical analysis techniques have limited theoretical justifications, and therefore no one can assert that they are risk-less, or even efficient.

#### 4.1.5.2. Financial Risks Estimation and Hedging

Popular models in financial mathematics usually assume that markets are perfectly liquid. In particular, each trader can buy or sell the amount of assets he/she wants at the same price (the "market price"). They moreover assume that the decision taken by the trader does not affect the price of the asset (the small investor assumption). In practice, the assumption of perfect liquidity is never satisfied but the error due to liquidity is generally negligible with respect to other sources of error such as model error or calibration error, etc.

Derivatives of interest rates are singular for at least two reasons: firstly the underlying (interest rate) is not directly exchangeable, and secondly the liquidity costs usually used to hedge interest rate derivatives have large variation in times.

Due to recurrent crises, the problem of risk estimation is now a crucial issue in finance. Regulations have been enforced (Basel Committee II). Most asset management software products on the markets merely provide basic measures (VaR, Tracking error, volatility) and basic risk explanation features (e.g., "top contributors" to risk, sector analysis, etc).

#### 4.1.5.3. Energy and Carbon Markets

With the rise of renewable energy generation (from solar, wind, waves...), engineers face new challenges which heavily rely on stochastic and statistical problems.

Besides, in the context of the beginning of the second phase (the Kyoto phase) in 2008 of the European carbon market, together with the fact that French carbon tax was scheduled to come into law on Jan. 1, 2010, the year 2009 was a key year for the carbon price modeling. Our research approach adopts the point of view of the legislator and energy producers. We used both financial mathematical tools and a game theory approach. Today, with the third phase of the EU-ETS, that didn't yet start, and the report form the Cour des Comptes (October 2013) that pointed out (among many others point) the lack of mathematical modeling on such carbon market design, we continue our research in this direction.

#### 4.1.5.4. Optimal Stopping Problems

The theory of optimal stopping is concerned with the problem of taking a decision at the best time, in order to maximise an expected reward (or minimise an expected cost). We work on the general problem of optimal stopping with random discounting and additional cost of observation.

#### 4.1.5.5. First hitting times distributions

Diffusion hitting times are of great interest in finance (a typical example is the study of barrier options) and also in Geophysics and Neurosciences. On the one hand, analytic expressions for hitting time densities are well known and studied only in some very particular situations (essentially in Brownian contexts). On the other hand, the study of the approximation of the hitting times for stochastic differential equations is an active area of research since very few results still are available in the literature.

#### **VERIDIS Project-Team**

# 4. Application Domains

#### 4.1. Application Domains

Distributed algorithms and protocols are found at all levels of computing infrastructure, from many-core processors and systems-on-chip to wide-area networks. We are particularly interested in the verification of algorithms that are developed for supporting novel computing paradigms, including ad-hoc networks that underly mobile and low-power computing or overlay networks, peer-to-peer networks that provide services for telecommunication, or cloud computing services. Computing infrastructure must be highly available and is ideally invisible to the end user, therefore correctness is crucial. One should note that standard problems of distributed computing such as consensus, group membership or leader election have to be reformulated for the dynamic context of these modern systems. We are not ourselves experts in the design of distributed algorithms, but we work together with domain experts on designing formal models of these protocols, and on verifying their properties. These cooperations help us focus on concrete algorithms and ensure that our work is relevant to the distributed algorithm community.

Our work on symbolic procedures for solving polynomial constraints finds applications beyond verification. In particular, we have been working in interdisciplinary projects with researchers from mathematics, computer science, system biology, and system medicine on the analysis of molecular interaction networks in order to infer the principal qualitative properties of models. Our techniques complement numerical analysis techniques and are validated against collections of models from computational biology.