2017-00189 - Biochemical computing (research internship)

Level of qualifications required: Bachelor's degree or equivalent
Function: Internship Research

About Inria
Inria, the French National Institute for computer science and applied mathematics, promotes "scientific excellence for technology transfer and society". Graduates from the world’s top universities, Inria’s 2,700 employees rise to the challenges of digital sciences. With its open, agile model, Inria is able to explore original approaches with its partners in industry and academia and provide an efficient response to the multidisciplinary and application challenges of the digital transformation. Inria is the source of many innovations that add value and create jobs.

About the research centre or Inria department
Located at the heart of the main national research and higher education cluster, member of the Université Paris Saclay, a major actor in the French Investments for the Future Programme (Idex, LabEx, IRT, Equipex) and partner of the main establishments present on the plateau, the centre is particularly active in three major areas: data and knowledge; safety, security and reliability; modelling, simulation and optimisation (with priority given to energy).

The 500 researchers and engineers from Inria and its partners who work in the research centre’s 31 teams, the 100 research support staff members, the high-level equipment at their disposal (image walls, high-performance computing clusters, sensor networks), and the privileged relationships with prestigious industrial partners, all make Inria Saclay Île-de-France a key research centre in the local landscape and one that is oriented towards Europe and the world.

Context
This research internship position is offered at Inria Saclay IdF (https://www.inria.fr/en/centre/saclay) in the LIFEWARE project-team, in the framework of the ANR-MOST project BIOPYSY "Biochemical Programming System" in partnership with Franck Molina’s lab Sys2diag in Montpellier, France and Prof. Jieh-Hong Jiang, Dept. electrical engineering, National Taiwan University.

The LIFEWARE team (http://lifeware.inria.fr) develops the Biochemical Abstract Machine (BIOCHAM http://lifeware.inria.fr/biocham4) software for modeling, analyzing and now synthesizing biochemical reaction networks (CRNs), using methods from fundamental Computer Science and mathematics. The software developments are expected to be integrated in BIOCHAM.

The internship will be supervised by François Fages who has supervised 29 Ph.D. theses in his career, the last defended in May 2016, and who currently is 100% available with no Ph.D. student.

Assignment
General introduction: Cells compute, they process signals they receive from and emit to their environment, regulate their metabolism, and take decisions such as cell division, differentiation or migration. Understanding these processes is a central
difficulty in many applications in medicine, health and agriculture, and the ultimate
goal of molecular cell biology which we see as a grand challenge for computer
science. Unlike digital programs, biochemical computation involves state transitions
that are stochastic rather than deterministic, continuous-time rather than discrete-
time, poorly localized instead of well-separated in modules, and created by evolution
instead of by rational design. Based on recent results in computability, complexity and
computable analysis, we are developing novel synthesis methods for compiling mixed
analog-digital programs into enzymatic reactions, comparing the generated code to
natural evolved reaction networks, and making experiments with extensive validation
in non-living vesicles created by microfluidic devices at Sys2diag lab.

Objective of the research internship:
The objective of this internship is to develop robust design principles for biochemical
reaction networks (CRNs) and gain insights on natural biochemical networks through
synthesis of artificial biochemical circuits with the same function. The state-of-the-art
in synthesis is to measure parameter sensitivity indices and optimize robustness after
the design. Depending on the skills of the candidate, the work will focus more on

- the computational theory of dynamical systems,
- the definition of low computational complexity classes for CRNs,
- robust design patterns for CRNs,
- high-level specifications of the function of natural CRNs (e.g. from the
  BioModels repository http://biomodels.org) with comparison between natural
  and synthesized CRNs for the same function,
- or realization of novel designs for biosensors with in vitro evaluation.

In all cases, in silico experiments and developments will be preferably done in the
BIOCHAM modeling environment, and some in vitro experiments will be possibly done
in tight collaboration with our Sys2diag partner.

Main activities

Our first compilation principles are described in the following paper

Fages, François, Le Guludec, Guillaume and Bournez, Olivier, Pouly, Amaury. Strong Turing Completeness of Continuous Chemical Reaction
Networks and Compilation of Mixed Analog-Digital Programs. In CMSB'17:
Proceedings of the fifteenth international conference on Computational Methods
in Systems Biology, pages 108–127, volume 10545 of Lecture Notes in
Computer Science. Springer-Verlag, 2017. [preprint http://hal.inria.fr/hal-
01519828]

and implemented in BIOCHAM v4 for compiling a mathematical function defined by a
Ordinary Differential Equations (ODEs). A demonstration notebook is available online
at http://lifeware.inria.fr:8888/notebooks/examples/cmsb_2017

We believe that these preliminary results have opened an whole avenue of research
with very nice results in several directions. The candidate will benefit from an
exceptional environment to develop his/her research among the points mentioned
above.

Skills

This subject requires common and basic knowledge on ordinary differential equations,
computability theory and complexity. The candidate will have to be fluent in English.

There is no specific prerequisite for this Thesis. However, some specific knowledge on
either analog computing, differential dynamical systems, circuit verification, circuit
synthesis, VHDL-AMS, Prolog, systems biology, synthetic biology, or chemistry will be
a plus.

Benefits package

- Subsidised catering service
- Partially-reimbursed public transport
- Social security
- Paid leave
- Flexible working hours
- Sports facilities

Remuneration

500 euros/month + living compensation for foreigners