Project template

Lead institution/organization: Inria
Head of institution/ organization: Bruno Sportisse
Branch concerned: Inria Nancy – Grand Est
Academic region: Grand Est

Envisaged partner institutions/organizations: *if applicable*

Project title: AI for the simulation of molecular interactions towards the design of inhibitors for therapeutic usage
Acronym: IA-SIMIT
Keywords: Numerical simulation, molecular interaction, artificial intelligence, therapeutic molecules, inhibitors.

Expected duration: 5 years

Scientific theme: Digital Biology

Corresponding CNU/CoNRS/CSS section(s): Sections CNU 27, 64, CoNRS 6, 20, 13, 16

Strategy of the lead institution:

This Chair aims to support and intensify the work of CAPSID, one of the 12 Inria project-teams in the field of Digital Biology, in line with Inria Nancy – Grand Est's local partnership strategy with Université de Lorraine. In doing so, it contributes to two central goals of Inria: i) to create and develop research at the crossroads of digital sciences and other disciplines, in order to foster major scientific advances and the emergence of new, unexplored scientific fields, and ii) to increase the technological readiness level of the resulting software beyond scientific proofs-of-concept through a close connection with end-users, in order to achieve a concrete impact on all disciplines at stake and to provide a solid basis for industrial transfer or clinical use. At the same time, Inria is betting on these new links across disciplines to build and offer original training programs combining solid fundamental knowledge and experimental practice in several disciplines. The Chair also contributes to Inria's international attractiveness strategy.

Strategy of the hosting laboratory:

The chair aims to strengthen the CAPSID project-team, common with CNRS and Université de Lorraine within the Lorraine Laboratory for Research in Computer Science and its Applications (LORIA, UMR 7503), and to intensify its collaboration with the Laboratory of Theoretical Physics and Chemistry (LPCT, UMR 7019) regarding the integration of experimental results in numerical simulations in biophysics on the one hand, and with the Laboratory of Molecular Engineering and Articular Physiopathology (IMoPA, UMR 7365) regarding the validation of active molecules and their therapeutic applications on the other hand. This is in line with Inria Nancy – Grand Est's desire to contribute fully to Université de Lorraine's overarching strategy on "systemic engineering". Inria Nancy – Grand Est aims to promote, support and develop multidisciplinarity around digital science and technology, in support of

Université de Lorraine's strengths, including the field of health. The training aspect of the Chair will contribute to Université de Lorraine's ORION program which aims to offer students from different disciplines more opportunities to mix with each other.

Summary of the scientific project:

The Chair's scientific project is at the crossroads of the fields of structural bioinformatics, digital simulation of biophysical systems and artificial intelligence (AI), with applications to the field of health. This involves proposing, implementing, and evaluating innovative AI-based approaches for the design of new therapeutic molecules, capable of mimicking and/or inhibiting protein interactions, such as virus-receptor interactions that allow the propagation of viruses. The design of suitable data-driven AI methods for the modeling and design of molecular interactions will be based in particular on deep neural networks, on representation learning by auto-encoders, and on the modeling of interactions by molecular graphs. Many challenges are to be addressed, from the acceleration of software for the dynamic simulation of molecular interactions, the modeling of the flexibility of biological molecules (proteins, peptides) by ensemble methods, and the calculation of binding free-energy from simulations, to the prediction of active molecules by their ability to inhibit harmful interactions.

Summary of the teaching project:

The Chair's teaching project will have a strong multidisciplinary flavor. It will target both students in digital sciences and in biology, by providing the former with health-related applications borrowed from biophysics or structural bioinformatics, and the latter with essential notions of digital sciences to understand the AI methods used in various fields of study, including for the design of therapeutic molecules. The relevant educational branches at Université de Lorraine which are already aware of this type of multidisciplinarity include the IAMD program ("Artificial Intelligence and Big Data") for engineering students from Telecom-Nancy, the "Molecular Biology and Applications" course at the Industrial Engineering and Applied Mathematics Department of Mines Nancy, the Biology-Health-Environment Master-Engineer Curriculum (CMI BSE), the Molecular Engineering option of the Master of Biotechnologies, etc. The medium-term objective is to create a joint educational program across two or more branches, in order to promote cross-disciplinarity.

Financial summary:

In addition to the Chair holder's salary, the budget required to carry out the scientific project includes:
- 1 PhD student for 36 months (120 k€)
- 1 post-doctoral fellow for 24 months (96 k€)
- operating costs: 1 laptop, internships, travel costs (34 k€)

This amounts to a total of 250 k€. A 50 k€ co-funding request will be submitted to the Grand Est Region within the framework of their existing AI PhD co-funding program. We are requesting a funding of 200 k€ from ANR.

Total CPJ funding (including ANR package)	498 k€
Co-funding	87 k€
Total funding	585 k€

Scientific dissemination: The results will be published in leading journals in the field of Computational Biology, for example:

- Nature Scientific Reports
- PLOS Computational Biology
- Proteins
- Journal of Chemical Information and Modeling

The Chair holder will participate in the CAPRI (Critical Assessment of Prediction of Interactions) challenge: https://www.ebi.ac.uk/pdbe/complex-pred/capri/.

Open science: The Chair fosters an open science approach, which can be implemented according to the following principles.

- Implementation of a DMP (Data Management Plan) based on the Opidor model
- Release of datasets and relevant metadata in DOREL (Université de Lorraine's repository for research data) to obtain a permanent DOI-like identifier.
- Release of software on a public GIT platform under an open source (MIT-like) license. High-TRL software will also be archived in Software Heritage.
- Publications in Open Access journals and dissemination of all papers on the HAL public archive.

Science and society: The Chair holder and the other participants will speak at general audience events such as the Fête de la Science, Salon Cité-Santé, or the AI and Health symposium organized each year by CHRU Nancy, to explain the project and raise awareness of the innovative approaches being developed and (at the end of the project) the results achieved.

KPIs : Possible KPIs include:

- Presentation of the DMP
- Hiring of a PhD student and a post-doctoral fellow
- Effective supervision, attested by the publications and talks of the PhD student and the post-doctoral fellow
- Effective release of software and datasets
- Effective collaboration between the Chair holder and the LPCT and IMoPA laboratories, attested by joint supervision or joint publications
- Habilitation degree obtained by the Chair holder
- Presentation of the a joint educational program across two or more branches.
- A shared space will be setup on mybox.inria.fr or bul.univ-lorraine.fr in order to store all the documents relating to the Chair and to be able to monitor these KPIs. A committee will be setup to monitor progress on a yearly basis, in the presence of all participants and representatives of the organizations involved.