A propos du centre ou de la direction fonctionnelle

Grenoble Rhône-Alpes Research Center groups together a few less than 800 people in 35 research teams and 9 research support departments.

Staff is localized on 5 campuses in Grenoble and Lyon, in close collaboration with labs, research and higher education institutions in Grenoble and Lyon, but also with the economic players in these areas.

Present in the fields of software, high-performance computing, Internet of things, image and data, but also simulation in oceanography and biology, it participates at the best level of international scientific achievements and collaborations in both Europe and the rest of the world.

Contexte et atouts du poste

Within the framework of a partnership

- the project will be conducted within public partnership with European and French organizations located in Grenoble (ESRF, ILL, EMBL, and IBS)

Mission confiée

For a better knowledge of the proposed research subject:

Despite the exponentially growing amount of biological macromolecules solved with various experimental techniques such as X-ray crystallography, nuclear magnetic resonance (NMR), or cryo-electron microscopy (cryo-EM, cf. 2017 Nobel Prize in Chemistry, Eisenstein 2016), our understanding of their structural organization still lags behind the amount of structures. This is mostly due to the combinatorial explosion of possible interactions involved, even though the fundamental forces between atoms and molecules are almost fully understood at a theoretical level and classical computer simulations have become an integral part of research activities in academic and industrial chemistry (cf. 2013 Nobel Prize in Chemistry). The practical application of these methods to large biomolecules faces important practical difficulties due to the very large size of the molecular conformational space and the dynamic nature of biologic structures (Shaw et al. 2008).

Very recently, data-driven algorithms equipped with artificial intelligence have made a big leap forward in the field of computational structural biology. Indeed, as John Moult, the lead organizer of the CAPS large-scale community-wide experiment to assess protein structure prediction methods, announced at the CAPRI 13 congress in the beginning of December 2018, "the problem of protein structure prediction from its sequence has been essentially solved"(AlQuarishi 2018). This was made possible thanks to the rapid progress in multiple experimental and computational disciplines. These include-techniques, algorithms for multiple sequence alignment, statistical methods to analyze sequence profiles, sufficient amount of 3D protein structures in structural databases, and artificial intelligence methods together with the corresponding hardware. However, under physiological conditions, biological molecules, such as proteins, are not rigid, and very often have multiple functional states (Gerstein & Echols 2004) or exhibit a significant amount of flexibility (structural heterogeneity) (Nogales 2016). This structural heterogeneity is not occasional and is frequently linked with specific biological function (Williams 1979; McCammon & Karplus 1983; Teitell et al. 2011, Tang & Dill 1998; Fields 2001). For example, it can be evolutionary designed for signal transduction or binding of proteins with other molecules (such as proteins, RNAs, DNAs, or small ligands). Therefore, our ability to predict and explain conformational transitions in macromolecules and how they bind with other molecules is crucial for understanding fundamental mechanisms of life machinery.

The future challenges of the structural bioinformatics community will thus be predictions of multiple functional states of the same protein, prediction of protein flexibility, prediction of how proteins interact with each other, with small molecules, how they form assemblies (the protein docking problem), and ultimately protein design for specific function. All of these problems are currently very difficult to solve without using additional information. A tractable approach will be to complement ab initio computations with (i) sparse experimental data (these can be pieces of information from multiple experiments) and (ii) information from genomic and structural databases. This constitutes the essence of modern integrative structural biology - a combination of physics-based and knowledge-based approaches with all available experimental information, which can be sparse and ambiguous.

The goal of the project is to develop novel modules for sparse experimental data (Cryo-EM constraints and mass-spectrometry, for example), add data-driven constraints (co-evolution, distance matrices, etc), and more importantly, develop robust sampling techniques based on the state-of-the-art in Monte-Carlo, swarm optimization, and Bayesian statistics. These will be integrated into the simulation pipeline developed in the team. More examples can be found at https://team.inria.fr/nano-d/software/.

Informations générales

- Thème/Domaine : Schémas et simulations numériques
- Ville : Grenoble
- Centre Inria : CRI Grenoble - Rhône-Alpes
- Date de prise de fonction souhaitée : 2019-10-01
- Durée de contrat : 11 an, 4 mois
- Date limite pour postuler : 2019-04-28

Contacts

- Equipe Inria : NANO-D-POST
- Recruteur : Grudinin Sergey / sergei.grudinin@inria.fr

A propos d'Inria

Inria, l’institut national de recherche dédié aux sciences du numérique, promeut l’excellence scientifique et le transfert pour avoir le plus grand impact. Il emploie 2400 personnes. Ses 200 équipes-projets agiles, en général communes avec des partenaires académiques, impliquent plus de 3000 scientifiques pour relever les défis des sciences informatiques et mathématiques, souvent à l’interface d’autres disciplines. Inria travaille avec de nombreuses entreprises et a accompagné la création de plus de 160 start-up. L’institut s’efforce ainsi de répondre aux enjeux de la transformation numérique de la science, de la société et de l’économie.

L’essentiel pour réussir

We are looking for talents in designing novel algorithms in C++, both physics-based and data-driven with an interest in biophysics and structural bioinformatics.

Consignes pour postuler

Starting date: 1st October 2019, duration: 16 months.

Applicants should hold a PhD defended after 1st September 2017.

Applications have to be made on-line on the Inria web site before end of 28th April.

Sécurité défense:

Ce poste est susceptible d’être affecté dans une zone à régime restrictif (ZRR), telle que définie dans le décret n°2011-1425 relatif à la protection du potentiel scientifique et technique de la nation (PPST). L’autorisation d’accès à une zone est délivrée par le chef d’établissement, après avis ministériel défavorable pour un poste favorable, tel que défini dans l’arrêté du 1425 relatif à la protection du potentiel scientifique et technique de la nation (PPST). L’autorisation d’accès à une zone à régime restrictif (ZRR) est délivrée par le chef d’établissement, après avis ministériel défavorable pour un poste favorable, tel que défini dans l’arrêté du 1425 relatif à la protection du potentiel scientifique et technique de la nation (PPST).

Politique de recrutement:

Dans le cadre de sa politique diversité, Inria accueille les personnes en situation de handicap.
Collaboration :
The recruited person will be in connection with experimental scientists and instrument responsibles at ESRF/ILL/EMBL/IBS institutes in Grenoble working with specific biological systems.

Responsibilities :
The person recruited is responsible for algorithmic and code development, benchmarking, and conducting joint computational experiments with data provided by experimental collegues.

Principales activités
Main activities :
- Design and implementation (C++) of novel algorithms
- Integration of novel algorithms into a simulation pipeline
- Designing simulation benchmarks
- Running simulations
- Writing technical reports and public tutorials

Compétences
Technical skills and level required :
- We are looking for candidates from a computer science / applied math / applied physics background with strong knowledge of applied maths and physics and an interest in biophysics
- Knowledge of C++ and Python is strongly required
- Parallel programming (e.g. multi-threading) will be an asset

Languages :
- Strong oral, written and interpersonal communication skills (working language: English – knowing French is a plus) are required

Other valued appreciated :
- Ability to work independently and with a team

Avantages
- Subsidized meals
- Partial reimbursement of public transport costs
- Leave: 7 weeks of annual leave + 10 extra days off due to RTT (statutory reduction in working hours) + possibility of exceptional leave (sick children, moving home, etc.)
- Possibility of teleworking (after 6 months of employment) and flexible organization of working hours
- Professional equipment available (videoconferencing, loan of computer equipment, etc.)
- Social, cultural and sports events and activities
- Access to vocational training
- Social security coverage

Rémunération
Gross salary: 2 653 Euros per month.