
Level of qualifications required: Graduate degree or equivalent

Fonction: PhD Position

About the research centre or Inria department

The Inria Sophia Antipolis - Méditerranée center counts 37 research teams and 9 support departments. The center’s staff (about 600 people including 400 Inria employees) is composed of scientists of different nationalities (250 foreigners of 50 nationalities), engineers, technicians and administrators. 1/3 of the staff are civil servants, the others are contractual. The majority of the research teams at the center are located in Sophia Antipolis and Nice in the Alpes-Maritimes. Six teams are based in Montpellier and a team is hosted by the computer science department of the University of Bologna in Italy. The Center is a member of the University and Institution Community (ComUE) “Université Côte d’Azur (UCA)”.

Context

Keywords: molecular simulation, flexibility, conformational space, exploration, coordinated moves, thermodynamics.

Context: Interactions between biomolecules (proteins, nucleic acids) are dynamic processes involving conformational changes. These conformational changes allow the partners to adapt to one another – a property which is key for selected proteins to accomplish several functions. As of today, predicting large amplitude conformational changes, such as for example a coil-to-helix transition during the association of two proteins, is an open problem. Predictions often consist in applying so-called move sets which locally deform the molecule. Alas, designing move sets is especially challenging due to the condensed nature of proteins; compactness indeed imposes a game of musical chairs, since atoms must move in a coordinated fashion so as to avoid steric clashes.

Scientific environment: The Algorithms-Biology-Structure project team, from Inria Sophia Antipolis (https://team.inria.fr/abs/) is a leading team for the development of advanced algorithmic methods in computational structural biology, and for their implementation.

Assignment

Goals: The goal of this PhD thesis will be to design novel move sets able to predict reliably large conformational changes for condensed environments in general and for proteins in particular. The methods developed will borrow from novel correlation analysis for known structures, and from novel kinematic analysis in complex configuration spaces. The methods will be implemented in the Structural Bioinformatics Library (SBL, http://sbl.inria.fr), an advanced C++ environment providing both low level algorithms and end-user applications for computational structural biology [CD17].

In a second step, the methods will be coupled to state-of-the art exploration and analysis algorithms for energy landscapes [RDRC16, CDM+ 15, CMCW16] developed in the group. This coupling will make it possible to test them on complex molecular machines (membrane proteins, polymerases of viruses, cargo proteins), so as to make a stride towards the understanding of mechanisms accounting for their function at the atomic scale.

References


Main activities
The main activities will be threefold: designing and analyzing algorithms, implementing them in advanced generic C++, and testing them on challenging molecular machines.

Skills
Background: Master in structural bioinformatics or biophysics or bio-mathematics or computational chemistry or computer science.

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

Remuneration
Duration: 36 months
Location: Sophia Antipolis, France
Gross Salary per month: 1982€ brut per month (year 1 & 2) and 2085€ brut/month (year 3)