M2 Sciences des Matériaux et Nano-Objets (SMNO)

Sorbonne Université, ENS Ulm, Chimie ParisTech, ESPCI, l'École Polytechnique

Proposition de stage 2018-2019

Laboratoire : Institut des nanosciences de Paris (INSP)
collaboration with the Laboratoire de chimie théorique (LCT)
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Nuclear quantum effects for biochemistry using polarizable force field

Accurate atomic scale simulations of the properties of water, which are central in biochemistry, remain a theoretical and practical challenge. This is due to two major difficulties: first, it requires an accurate description of the interatomic interaction at a reasonable computational cost, second, one needs to account for the quantum nature of the light nuclei. To address these two issues, we propose to use polarizable force fields (PFF) for the interatomic interactions [1] in combination with quantum thermal bath (QTB) and/or path-integral molecular dynamics (PIMD) for the modelization of the nuclear quantum delocalization [2,3].

Biochemical simulations usually involve big systems such as proteins made of thousands of atoms in solutions with tens of thousands of water molecules. This makes it impossible to use *ab initio* approaches, based on quantum electronic calculations: the only computationally reasonable way to model these systems is through classical models for the description of the interatomic interactions. In most of these classical models, the interaction between atoms consist in harmonic bonded terms combined with Van der Waals and electrostatic non bonded terms. It means that these descriptions don't take into account the electronic mobility, corresponding to a response of the system to a change in the environment. This can be corrected by adding to the potential a many-body term modelling polarization effects, at the additional computational cost of solving self-consistent equations at each time step of the simulation. This has led, in recent years, to the apparition of several polarizable classical models (force fields) whose parameters are calibrated against electronic structure reference calculations. However, it has been shown that the properties obtained with these PFF models are surprisingly not accurate for many systems if nuclear quantum effects (NQEs) are not taken into account in the simulations [4].

In the majority of atomistic numerical simulations, the nuclei are considered as classical particle. This is not always valid, especially for light nuclei such as hydrogen. Different methods have been developed to account for nuclear quantum effects (NQEs) in molecular dynamics simulations. The most widespread approach, PIMD, is based on Feynman path-integrals formalism. In PIMD simulation, each atom is replaced by a ensemble of replica, coupled by harmonic springs. This method provides an exact reference for thermodynamic properties, while taking into account NQEs, but the necessity to replicate the system implies a significant numerical overcost with respect to classical nuclei simulations. In the QTB approach, on the other hand, the quantum indeterminacy is mimicked via a Langevin equation with a suitable random force (the "bath"). This methods is an interesting alternative to PIMD since it accounts approximately for the NQEs, with a computational cost that remains comparable with that of classical simulations.

During the internship, the student will implement QTB and PIMD methods within the massively parallel software Tinker-HP, in order to study NQEs in realistic biological system using accurate PFF.

[1] L. Lagardère et al., Tinker-HP: a massively parallel molecular dynamics package for multiscale simulations of large complex systems with advanced point dipole polarizable force fields, **Chem. Sci.**, 2018, **9**, 956-972
[2] Hichem Dammak, et al. Quantum Thermal Bath for Molecular Dynamics Simulation. Phys. Rev. Lett.,**103,** 190601, 2009.
[3] T. E. Markland, M. Ceriotti, Nuclear quantum effects enter the mainstream, arXiv:1803,01037 (2018).
[4] L.Pereyaslavets et al., On the importance of accounting for nuclear quantum effects in ab initio calibrated force fields in biological simulations, PNAS (2018).

Techniques utilisées : Molecular dynamics, quantum statistical mechanics, fortran programming
Rémunération éventuelle du stage : Yes
Possibilité de poursuivre en thèse : Yes, possibly
Si oui, mode de financement envisagé : Ecole doctorale