Computational Approaches for Bio-marker Design: A three-levels learning workshop

Computational approaches are used in all areas of science, engineering, medicine and materials-science due to their inexpensive and non-destructive procedures to solve problems. In this workshop, we will discuss about the methods for modeling the biomarkers that are useful in health-care applications as diagnostic agents. We will cover the fundamental theories behind the computational methods relevant for modeling the structural and spectroscopic properties of biomarkers, and some coding to implement some of the learned principles and finally some application works using the available softwares. Overall, we cover all the essential parts of computation namely : **theory, coding and applications**. Some basic-level knowledge in programming is essential to follow the coding part of the workshop. Otherwise, the students are welcome to participate solely in the theory and application sessions of the workshop. The preferable language for programming is **Fortran** but participants are free to use any language (or scripts) with which they are comfortable.

PS: Eventhough the title of workshop appears too-specific, the topics covered can be useful for any students/researchers interested in modeling the (linear and non-linear) optical properties of organic/inorganic molecules in solvents, bio or any heterogeneous environment.

Preliminary schedule

	Monday	Tuesday	Wednesday	Thursday	Friday
Lectures	1.5 h	1.5 h	1.5 h	1.5 h	1.5 h
Hand–on sessions	2 h	2 h	2 h	2 h	2 h
Coding	1–2 h	1–2 h	1–2 h	1–2 h	1–2 h

1 Concepts

- **Motivation:** Why computational approaches?
- **Theories behind:** The theories for understanding properties of atoms, organic and biological molecules and materials: quantum mechanics, classical mechanics and statistical thermodynamics
- **The silicon way:** Computational approaches to understand atoms, molecules and materials

  1. *Static approaches:* Molecular mechanics, electronic structure methods
  2. *Dynamics approaches:* Force-field and ab initio based approaches such as molecular dynamics, Monte Carlo approaches, Born-Oppenheimer MD, Car-Parrinello MD

- **Nothing is in vacuum:** Modeling condensed phase systems :

  1. *Implicit approaches:* Generalized Born and Poisson-Boltzmann, Polarizable continuum

2. Explicit: Monte Carlo, molecular dynamics and hybrid Quantum mechanics/molecular mechanics (QM/MM) molecular dynamics

- **Let there be light:** Modeling the light-matter interaction: Time-dependent approaches(TDHF and TD-DFT)
- **Facing the reality:** Theory for extended systems interacting with light : Hybrid QM/MM (TD-DFT/MM) response

2 Application

Computing the linear and non-linear optical properties of a probe molecule

- (i) How to create coordinates for a molecule (use **MOLDEN**)
- (ii) To get the optimized geometry and compute charges in a particular solvent (use **GAUSSIAN**)
- (iii) Prepare the solute-solvent initial configuration (use **Ambertools**)
- (iv) Run MD for the solute-solvent system (use **AMBER12**) with Rigid and flexible solute
- (v) Analyze the solute-solvent structure and prepare QM/MM input files
- (vi) Run QM/MM calculations to compute OPA and TPA properties (use **DALTON**). Let us refer the results for rigid solute as (vi-a) and for the flexible solute as (vi-b)
- (vii) Use trajectory from hybrid QM/MM MD and compute the properties.

Write a report by comparing the results from vi-a, vi-b and vii. The results from which of this set agree to experiments and why?

3 Coding

- Write a Monte Carlo program for calculating the value of π.
- Write a Monte Carlo program to find the minimum energy structure of Lennard-Jones Cluster. The importance of initial configuration- simulated annealing- genetic algorithm
- Write a Monte Carlo code for argon liquid (in NVT ensemble) : Initial structure, minimum image convention, periodic boundary condition, energy calculation
- Write a Molecular dynamics code : Algorithms to integrate Newton's equation of motion, various integrators, force calculation
- Code analysis: Write programs to compute structural and dynamical quantities, rdf, MSD, VACF
- A simple code to do Hartree-Fock calculation