ESDW6: Classical MD

Location: CECAM-NL
Webpage: https://www.cecam.org/workshop-0-1406.html
Dates: August 14, 2017 to August 25, 2017
Organizers: Peter Bolhuis (University of Amsterdam, The Netherlands), Christoph Dellago (University of Vienna, Austria), David Swenson (University of Amsterdam, The Netherlands)

1 State of the art

During the past decades, classical molecular dynamics (MD) simulation has become a central tool in many branches of science and engineering. In particular, in molecular biology, chemistry, and materials science, MD simulations routinely provide insights into molecular mechanisms with a spatial and temporal resolution not accessible to experimental probes. Many software packages for MD simulations have been developed, opening the possibility to carry out such simulations to a broad community of researchers. However, the relatively short time scales accessible to MD still limit its applicability. This is particularly true for processes dominated by rare but important barrier crossing events, such as protein folding and binding, chemical reactions in solution, and nucleation.

In the last few years modeling of rare events has made tremendous progress and several computational methods have been put forward to bridge the time scale gap. In particular, the trajectory sampling methods, such as transition path sampling, transition interface sampling, and forward flux sampling, promise an accurate yet efficient solution to the rare event problem in complex systems. However, these new approaches have not yet been included, with adequate efficiency and scalability, in common simulation packages. This is mostly because their implementation and application requires specialized expert knowledge.

The goal of this workshop was to discuss the implementation of such methods and to create software modules that can be used in conjunction with existing programs to address the computational challenges caused by rare events. The workshop focused on the development of user-friendly modules to sample rare barrier crossing trajectories and to analyze their molecular mechanisms.

This workshop was organized in the classical molecular dynamics scientific pillar of E-CAM and focused on making state-of-the-art methods accessible to a broader audience by providing robust software modules.

2 Training provided

This workshop included 22 total participants, with 11 who participated in the development of modules, plus 10 senior participants, who gave instructional talks and provided advice on module development, and 1 participant from an E-CAM industrial partner.

The primary training came in the form of the development of software modules based on OpenPathSampling, which was how the majority of the time at the workshop was spent, beginning on the third day. The first few days were primarily talks to introduce essential background material, with a few other such talks interspersed over the rest of the two weeks.

These talks can be categorized by their primary focus: on science, on molecular dynamics software, or on general software development. They are described below.

Talks focused on scientific topics:

- Christoph Dellago gave an in-depth lecture on state of the art rare event sampling. This included an introduction to the basics of path sampling, as well as discussion of advanced path-based sampling methods.
- Jan-Hendrik Prinz gave a talk about a novel approach, called observable operator models, which makes connections between Markov state models and transition path sampling methods. This approach is still very much in development, and exposes limits in our current understanding of the connections between various methods in the field of classical molecular dynamics.
- Titus van Erp spoke about state-of-the-art methods and results for transition interface sampling, including novel path sampling moves that could be implemented as E-CAM modules. He also introduced the PyRETIS software package and demonstrated it, and demonstrated some applications of the methodology.
- Jocelyne Vreede presented about applications of path sampling methods, focusing on studies of biomolecular systems. Her presentation included work on signalling proteins, DNA, and oncogenic protein mutations.
- Peter Bolhuis discussed some cutting edge path sampling methods, as well as several possible future directions to handle remaining challenges. He highlighted a few remaining challenges for path sampling, including parallelization approaches and the need to develop better tools to extract reaction coordinates from the results of path sampling simulations.

Talks focused on molecular dynamics software tools:

- David Swenson showed how these state of the art path sampling methods could be used in OpenPathSampling (OPS), and gave an overview of how to add new tools for OPS.
- John Chodera introduced OpenMM, demonstrating how to use it to perform GPU-accelerated simulations of biomolecular dynamics, and also discussed some of the subtleties around choosing a molecular dynamics integrator.
- Gareth Tribello gave a talk about PLUMED, demonstrating the ways that it can be use to calculate order parameters.

Talks focused on general software development training:

- Jony Castagna introduced the ideas of object oriented programming as used in Python.
- Alan O'Cais gave a talk about software development best practices, introducing software development tools like GitLab and git. In addition, that talk discussed the E-CAM concept of "modules," which were the desired output of the workshop.
- Alan O'Cais gave a second talk, focused on effective use of HPC resources.
- David Swenson presented a tutorial on software testing for scientific programming, using the Python package nose.

3 List of software development projects

The following modules were developed at this workshop:

1. S-Shooting: An approach for calculating the rate of a reaction. It is similar to the reactive flux method, but instead of launching trajectories from constrained to a surface in phase space, it allows shots from a volume in phase space, which is easier to sample.
2. Spring shooting: A Monte Carlo move for transition path sampling. It aims to push the shooting point to be close to the transition state, which provides better sampling efficiency.
3. Web throwing: A Monte Carlo move for transition interface sampling. It aims to improve the decorrelation of trajectories, enhancing the exploration of trajectory space and therefore the efficiency of the algorithm.
4. PPTIS: Partial path transition interface sampling, a variant of transition interface sampling that is particularly useful for diffusive rare events.
5. PLUMED support: PLUMED is a powerful and widely-used package that can be used to calculate collective variables. This module creates an interface so that PLUMED can be used for collective variables in OpenPathSampling.
6. Shooting Range: A variant of the shooting move that selects shooting points from the region near the top of the barrier, in order to obtain better efficiency.

Of these, the Spring Shooting modules has already been accepted into the E-CAM Library, and S-Shooting was included in E-CAM Deliverable D1.3. The remaining modules will be included in future deliverables, after they are completed and included in the E-CAM Library.

4 Future plans

At the end of the workshop, six modules had made significant progress, with code mostly completed. We expect to have a follow-up meeting, to be held in Amsterdam for two days. Before the follow-up meeting, the participants are expected to complete the implementation of their modules, which as mostly done during the workshop. At the follow-up meeting, we will ensure that the modules meet E-CAM's quality standard for code, tests, and documentation. The documentation to be posted in the E-CAM library will be written, and, if possible, merged. At that point, these modules will be ready for inclusion in future E-CAM deliverables.