

Extended software development workshop (WP1: classical MD): trajectory sampling

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1. State of the art

During the past decades, classical molecular dynamics (MD) simulations have become an indispensable tool in many branches of science: in particular, in molecular biology, chemistry, physics, and materials science MD simulations are nowadays able to provide insights into molecular mechanisms with a spatial and temporal resolution that is not accessible to experimental probes and/or to *ab initio* computer simulations. Due to this capacity, classical MD simulations have also become a standard tool in industrial research, as for instance in the fields of materials design, biomolecular engineering, or drug design. The broad application of these simulation techniques is supported by the availability of related software packages, which rely on efficient and accurate implementations and which are regularly maintained, receiving on a regular basis methodological updates: LAMMPS, ESPRESSO, GROMACS and OPENMM are a few of these products that are available. Despite this progress, an even broader application of MD simulation is limited by the relatively short (real) times scales accessible to these techniques, a problem which becomes in particular apparent if the project at hand is characterized by substantially disparate time scales: thus rare, but important barrier crossing events, as they occur in protein folding, chemical reactions in solution or nucleation phenomena are still out of reach for standard MD simulations.

During the past two decades, considerable progress has been made in developing methods that allow detailed and reliable investigations of the above-mentioned processes. Only in recent time, groups of researchers have started to develop packages in the field of trajectory-based rare event simulations, however these products have not gained, so far, the broad distribution of standard MD program packages. The E-CAM state of the art workshop “Reaction Coordinates from Molecular Trajectories” (29 August – 2 September 2016, Leiden), helped to identify some specific software needs of the scientific community to overcome these problems. A scientific report from this workshop can be found [here](#).

The central goal of Work Package 1 (WP1) of E-CAM is to develop robust and efficient code for path based simulations for the simulation of rare event processes. This development is carried out within the framework of the OpenPathSampling package, which provides easy-to-use tools for performing transition path sampling simulations and analyzing the results, for instance in terms of committor distributions or collective variables. The underlying dynamics are generated using external MD engines such that it can be used in conjunction with available MD codes. Currently, support for OpenMM is available and development to support other MD engines, such as LAMMPS and Gromacs is underway.

2. Training provided

The first extended software development workshop of WP1 took place in Traunkirchen (Austria), from November 16 to 25, 2016. Among the 18 participants there were **ten experienced, senior researchers** and **eight junior participants**, recruited from some of the research groups of the senior researchers and from other groups interested using path sampling approaches in their research. The program contained, in particular during the first days, talks given by the senior researchers, providing an (i) overall view of the problem and (ii) focusing on the particular problems to be dealt with during the implementation phase of the workshop: overview was given on theories that provide the basis of how to simulate rare events in complex molecular systems and an introduction was made to the OpenPathSampling package. Complementary information was given on quantum nuclear effects in rare events and an industrial partner (from Biki Technologies) reported about the relevance of these simulation techniques in technological applications. These scientific presentations were complemented by more technical talks, dedicated to the GIT system, the software development guidelines developed for E-CAM, and tools for performance analysis of the codes.

3. Software development projects

The following software modules were defined at the beginning of the workshop:

- (i) Basic shooting and shifting algorithm
- (ii) Aimless shooting algorithm
- (iii) Reactive flux algorithm
- (iv) Calculation of the transition state ensemble
- (v) Maximum likelihood optimization of the reaction coordinate
- (vi) Optimal placement of interfaces for transition interface sampling

The junior participants chose one of the problems based on their own research interests and then worked on them individually or in teams of two. Close to 60 % of the workshop was then dedicated to the software development. Guided by the program manager (Jony Castagna) and two senior researchers (David Swenson and Donal MacKernan), the young researchers worked very efficiently: according the feed-back that was collected during the workshop on a regular basis, a progress in the code development was achieved that was beyond expectations.

Currently, the modules are finalized, adapted to the software development rules of E-CAM and tested. A round-up workshop will be held in Vienna (April 4 and 5, 2017), where these packages will be finalized such that they can be uploaded into the E-CAM repository for Classical MD. These modules will also be part of deliverable 1.3 of WP1.