ExTASY: A Python-based Extensible Toolkit for Advanced Sampling and Analysis in Biomolecular Simulation

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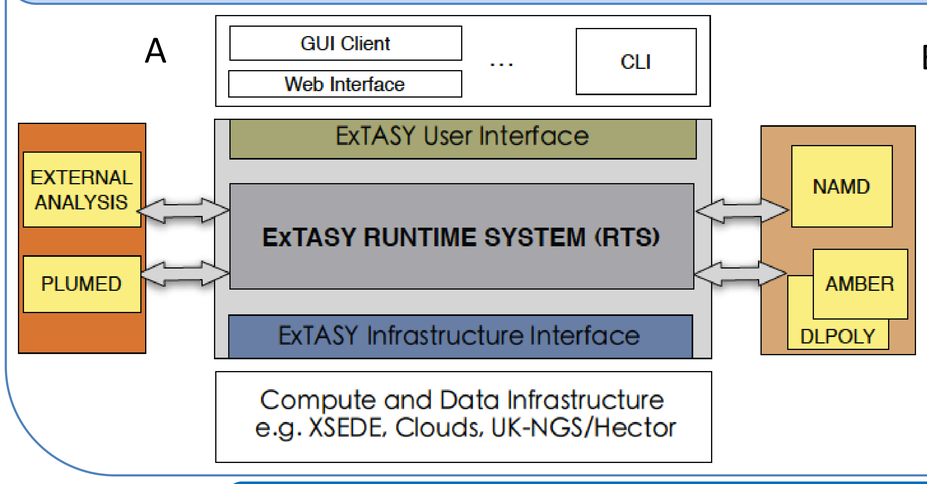
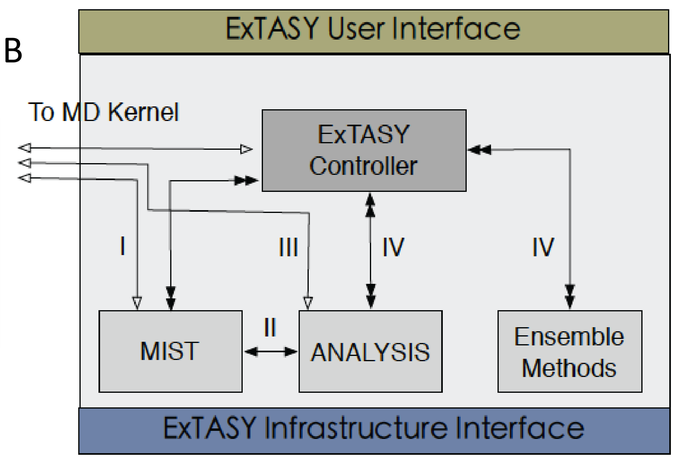
ExTASY

ExTASY - **Ex**tensible **T**ools for **A**dvanced **S**ampling and anal**Y**sis – is a project to provide the biomolecular simulation community with a **flexible** and **extensible** software **toolkit** of advanced sampling methods for **molecular simulation**, targeted primarily at High Performance Computing (HPC) infrastructures (www.extasy-project.org).

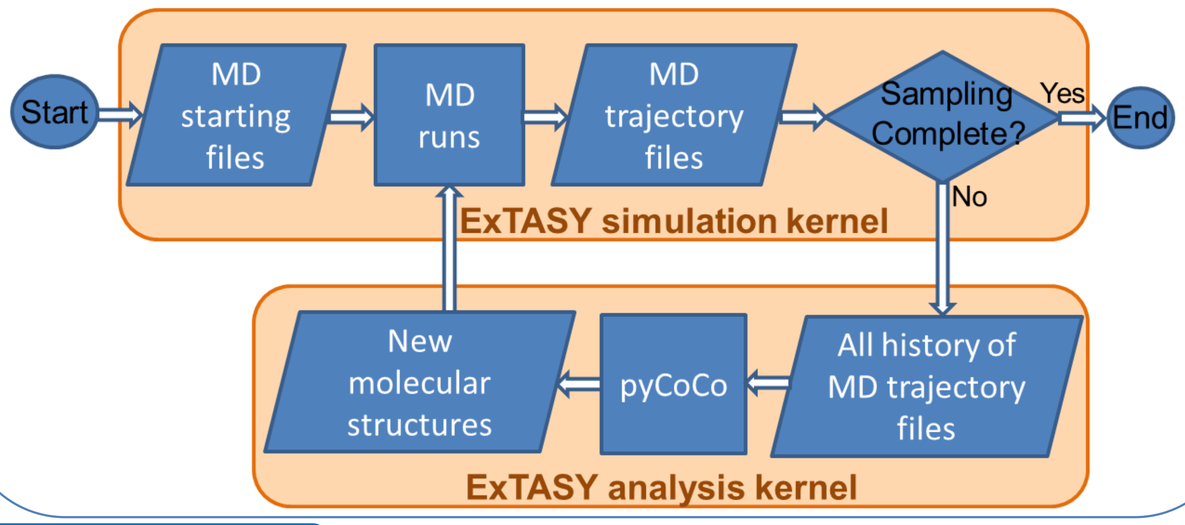




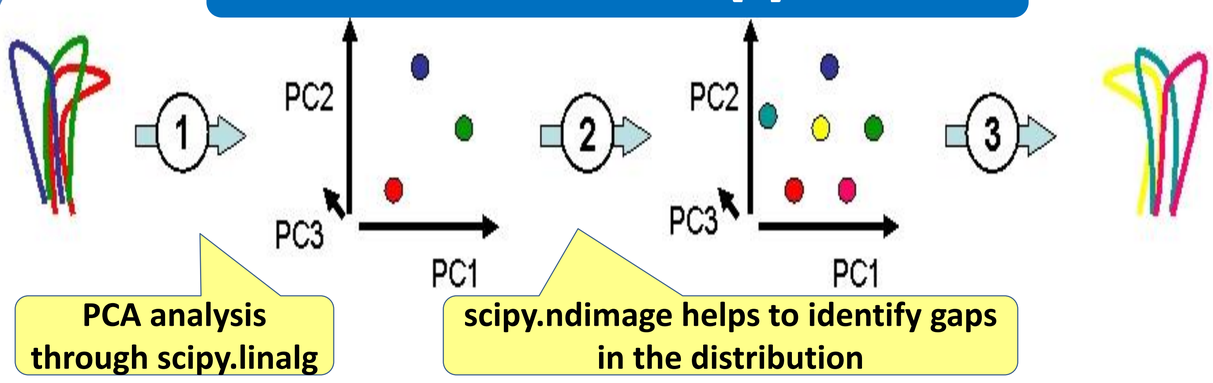
(A) Design of ExTASY. The modular elements that are developed or adopted are: **the ExTASY Runtime**, the **ExTASY interfaces** to the user and the infrastructure, and **plugins to community codes** and **analysis routines**.

(B) Architecture for the **ExTASY Runtime**, which defines the main components and the control flow between them. Closed double-headed arrows represent communication between components internal to ExTASY; arrows with open-heads represent communication from an ExTASY component to the Molecular Dynamics (MD) Engine. ExTASY uses SAGA-based Pilot-abstractions to provide fundamental support for ensembles, and SAGA to implement the infrastructure interface to different back-end systems.

CoCo-MD ExTASY workflow



CoCo method [1]

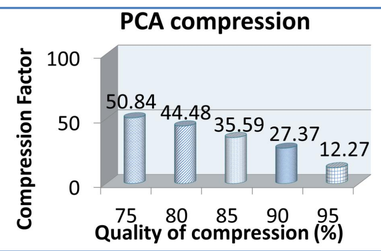


Analyses the distribution of a set of molecular structures in the shape space, and generates a new set of molecular structures that fills gaps in the distribution.

PCA

Principal **C**omponent **A**nalysis (PCA) applied to molecular simulation data:

- Reduces sampling data dimensionality in order to capture the dominant modes of motion of the molecular system;
- Gives insight into structural and dynamical behaviour of molecules;
- Enables highly compressed data storage of simulation trajectory files.



Python wise

- The Python-implemented **CoCo-MD** workflow maps molecular data structures into PCA space, identifies new data structures in the same space and converts the newly identified data structures back into the original dimensionality space of the MD data;

- MDAnalysis – a Python package – is used from CoCo-MD to convert MD data into **numpy** arrays that are subsequently processed in the code;

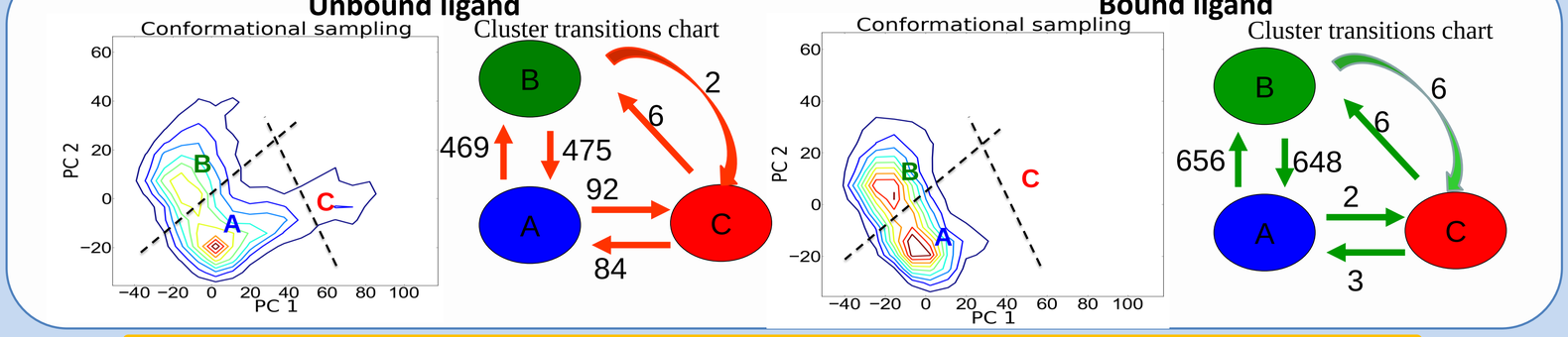
- scipy.linalg (linear algebra) is used to determine the PCA space of MD data – dimensionality-reduced space of the biomolecular system's shapes dynamics;

- **scipy.ndimage** (multi-dimensional image processing) is used to determine regions most distant from any sampled so far in the PCA space.

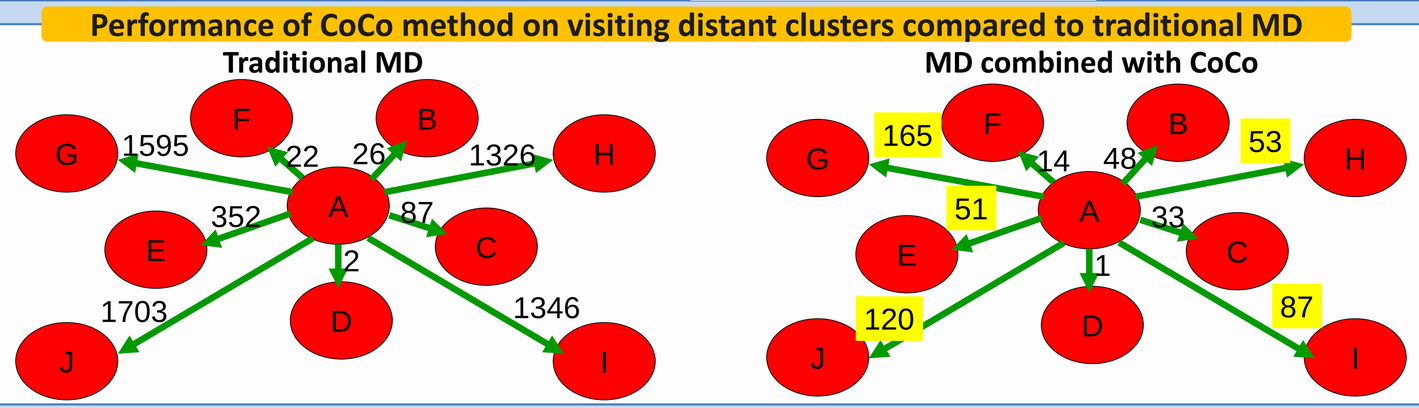
Results

- Results from the use of PCA to investigate the space of molecular shapes and transitions among them in the course of the MD simulations are shown for the Major Urinary Protein extending our previous work [2];
- Average of 100 independent simulations for each scenario;
- Dotted lines are the clusters boundaries of the PCA projections. Each of the clusters is assumed to belong to a specific molecular shape.
- The red circles A to J are the 10 clusters identified in the PCA projected space of simulation data of Penta Alanine;
- The labels of the green arrows show the number of steps that it takes before the cluster pointed by the arrow is visited from cluster A. Each step is associated with a print of a snapshot of atomistic coordinates in the course of the MD simulation.
- The CoCo method shows an excellent performance (yellow highlighted steps labels) on visiting the distant clusters much earlier than traditional MD.

Exploration of molecular shapes space and clusters of shapes transitions through PCA



Performance of CoCo method on visiting distant clusters compared to traditional MD



References

[1] Laughton C.A., Orozco M. and Vranken W. COCO: A simple tool to enrich the representation of conformational variability in NMR structures, PROTEINS, 75, 206-216 (2009) [2] Roy, J; Laughton, CA; *Biophys J.* ; 99(1): 218-226, 2010

Acknowledgements

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