

# OpenMMDL: A Workflow for Molecular Dynamics Simulations of Protein-ligand Complexes Setup, Simulation and Analysis

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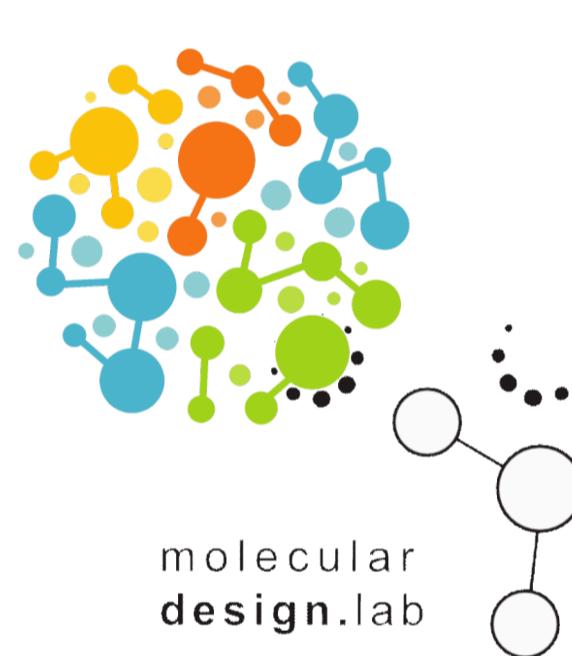
MD simulations in Computational Molecular Modeling:

- Explore protein-ligand interactions providing insights into the dynamics of essential biological interactions
- Predict drug binding and thus are often applied to optimize drug candidates
- Investigate cellular processes by exploring biological membrane dynamics
- Study protein folding, dynamics and conformation revealing structure-function insights

OpenMMDL presents an easy, intuitive and highly flexible user-friendly workflow for performing MD simulations

## Introduction

A workflow that is designed to ease the preparation, execution and analysis of OpenMM protein-ligand complex MD simulations for every single user.



## OpenMMDL

### Step I

Setup MD simulations with personally selected preferred parameters

### Step II

Perform OpenMM MD simulations with the following postprocessing

### Step III

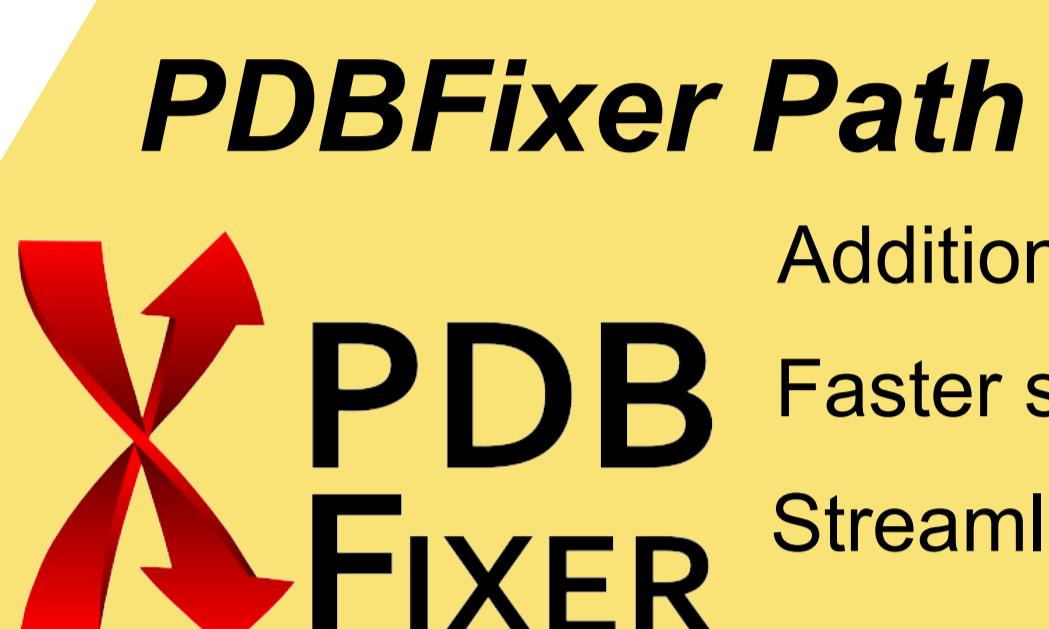
Analyze protein-ligand interactions

## Conclusion

The OpenMMDL workflow:

- Simplifies MD simulation setup for an easy and quick execution.
- Produces MD simulation input files via the PDBFixer and AMBER paths, allowing for flexibility.
- Performs an MD simulation with OpenMM followed by user-friendly postprocessing for simplified output analysis.
- Analyzes protein-ligand interactions across the entire MD simulation trajectory.
- Displays the different binding modes of the ligand and their transitions during the MD simulation.
- Generates a comprehensive 2D and 3D visualization of ligand-protein interactions.

## Step I OpenMMDL Setup



### Parameters:

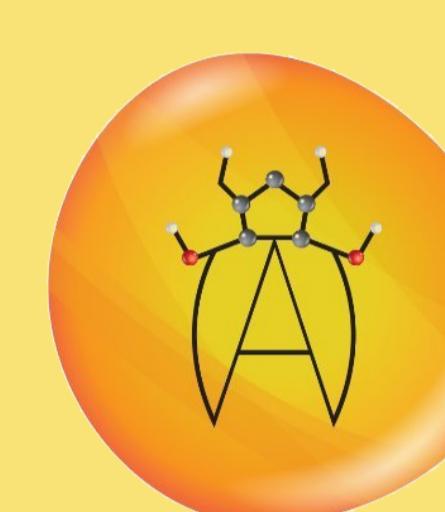
- Diverse selection of forcefield options for the protein and ligand
- Numerous water models and water box shapes and sizes
- Implemented equilibration and minimization protocol
- MD simulation length and time steps
- Number of frames in the trajectory
- MD simulation postprocessing
- Interaction analysis

### PDBFixer Path

- Additional OpenFF forcefield<sup>4</sup>
- Faster structure preparation
- Streamlined execution

- Two diverse ways of protein structure procession<sup>1,2</sup>
- Selection of system and simulation parameters<sup>3</sup>
- Generation of OpenMMDL Simulation files

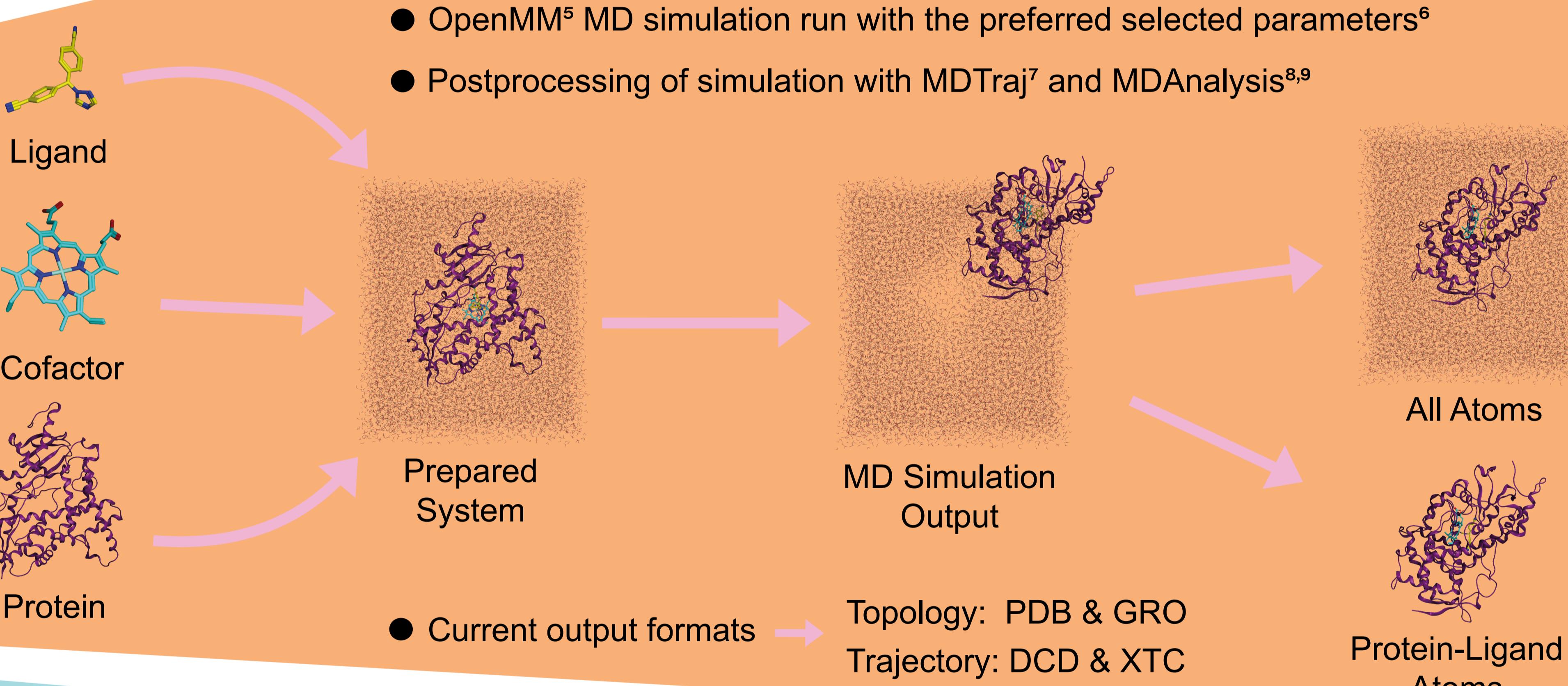
### Amber Path



- Increased forcefield type selection options
- Support of cofactors and special ligands
- Increased lipid type selection options
- Multiple ligands supported
- Lipid type mixtures

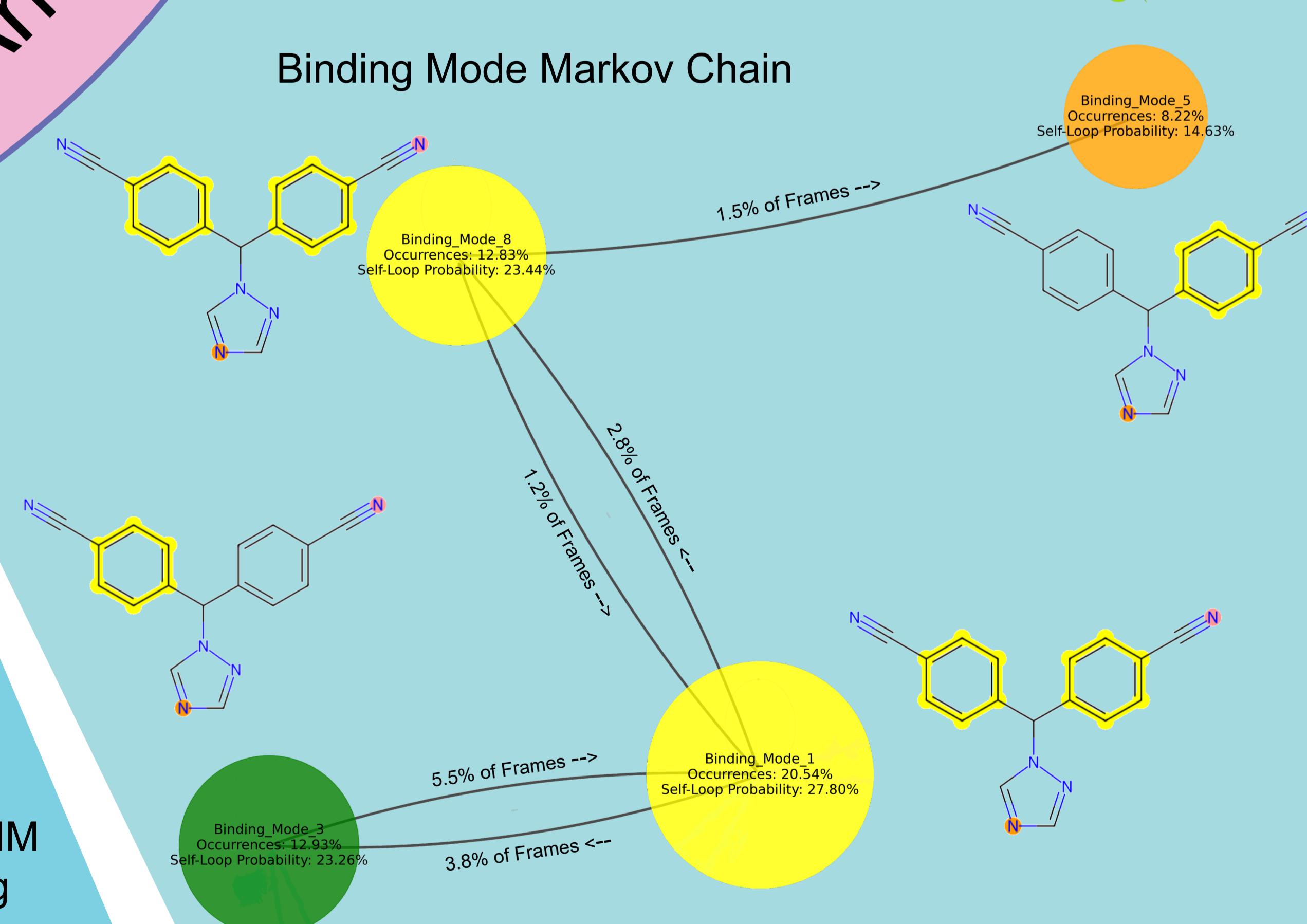
## Step II

## OpenMMDL Simulation

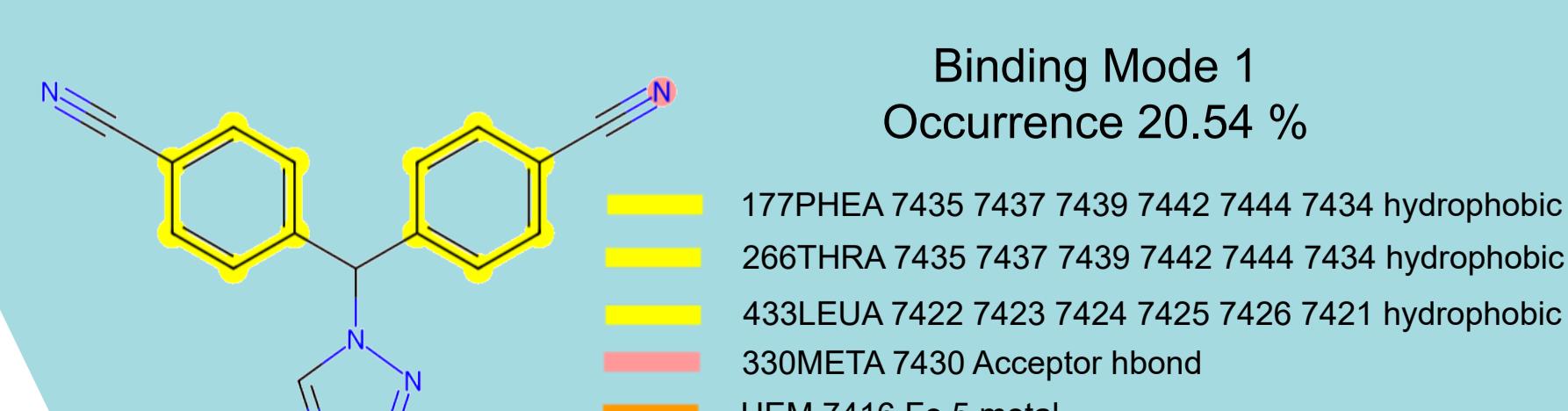


## Step III

## OpenMMDL Analysis



### 2D Binding Mode Visualization



- Interaction calculation with PLIP<sup>10</sup>
- Generation of interaction fingerprints for the whole trajectory
- Visualization of the fingerprints and interactions in 2D<sup>11</sup> and 3D<sup>12</sup>

### Interaction Barcode Generation



### 3D Interaction Visualization

