OpenMMDL: Building, Simulating, and Analyzing Protein–Ligand Systems in OpenMM

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molecular
design.lab

OpenMMDL

A Workflow for Molecular Dynamics Simulations of Protein-Ligand Complexes

Setup Simulation Analysis

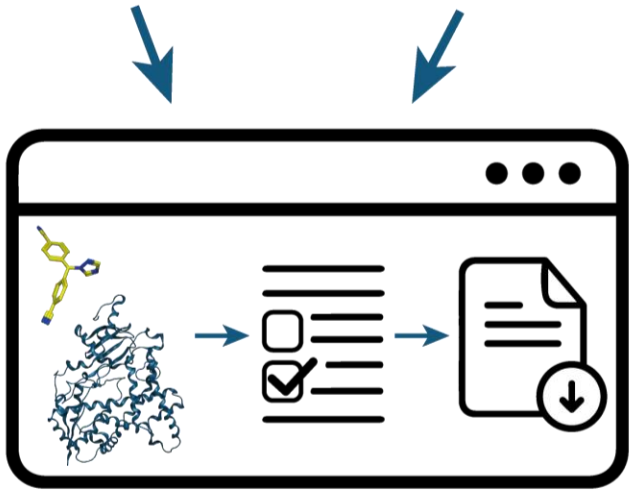
Setup

Simulation

Analysis

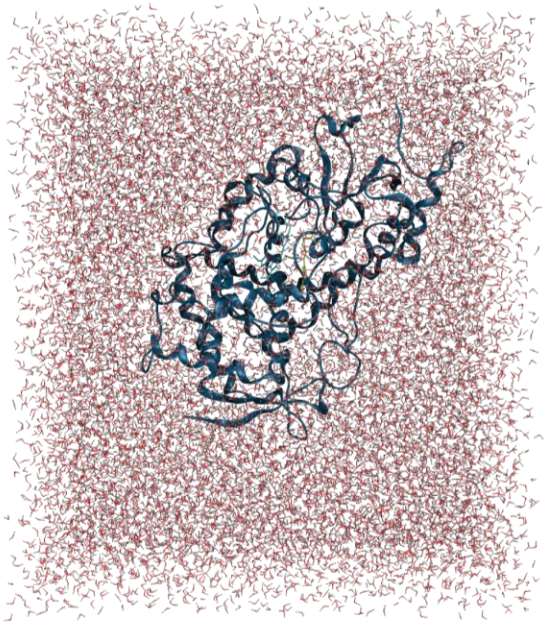
Setup

AmberTools PDBFixer



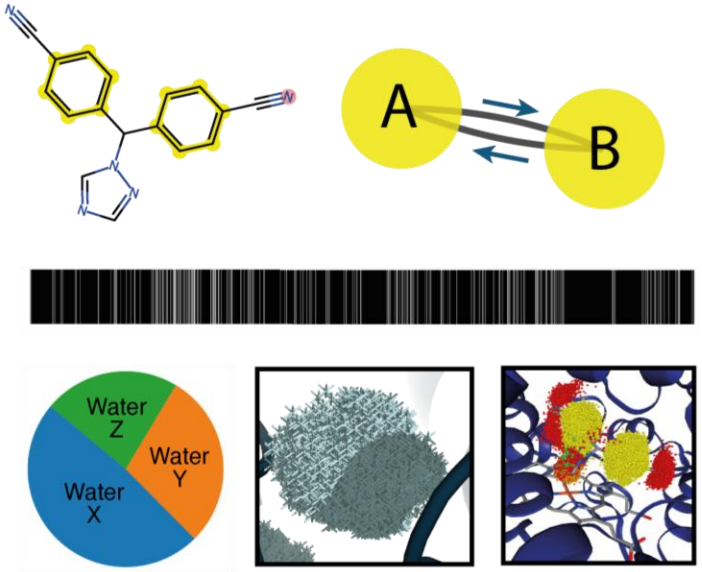
Structure-, System-
& simulation-configuration

Simulation



Preparation, Simulation
& Postprocessing

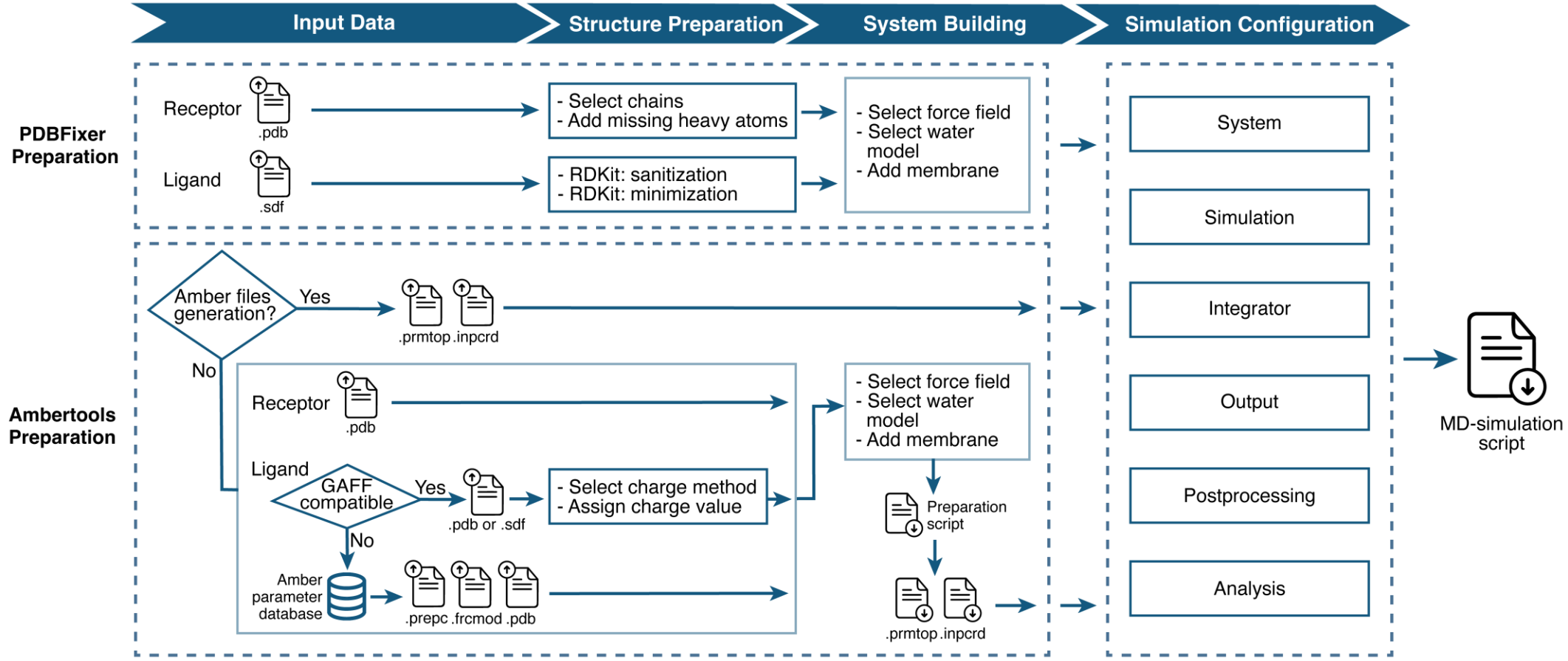
Analysis



Binding State Calculation,
Interaction Analysis,
& Water Bridge Calculation

Setup

- Flask based Web application
  - Based upon OpenMM Setup
  - Contains two preparation options
  - Adjustment of simulation settings



Setup

Simulation

Analysis

Setup

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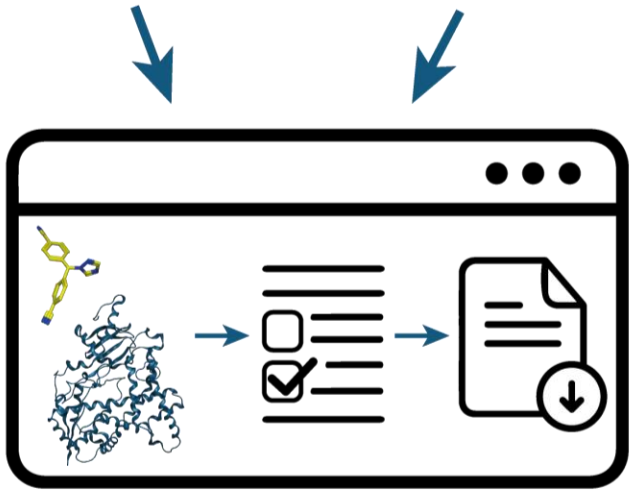

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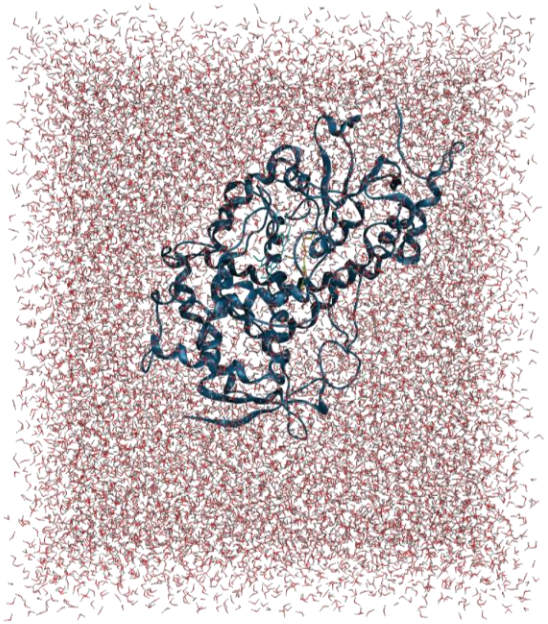
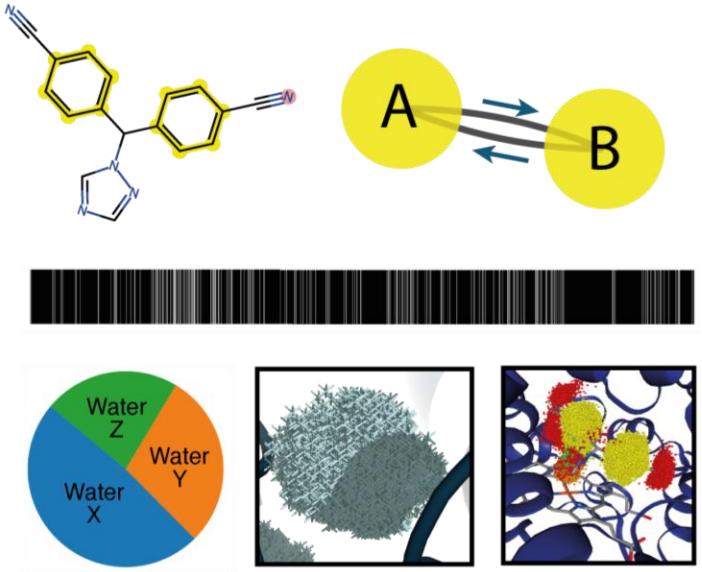
Simulation



Preparation, Simulation
& Postprocessing

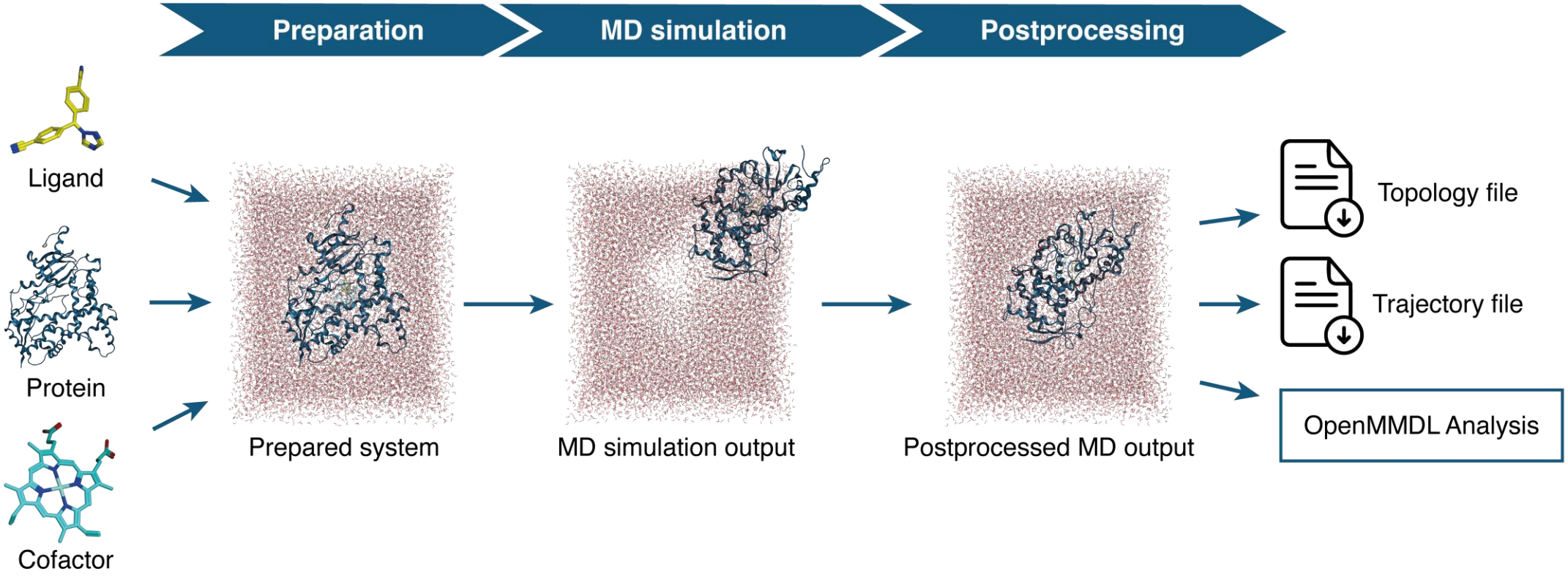
Analysis



Binding State Calculation,
Interaction Analysis,
& Water Bridge Calculation

Simulation

- Simulation with the settings obtained from Setup
  - Complex building
  - Postprocessing
    - MDTraj & MDAnalysis



Setup

Simulation

Analysis

Setup

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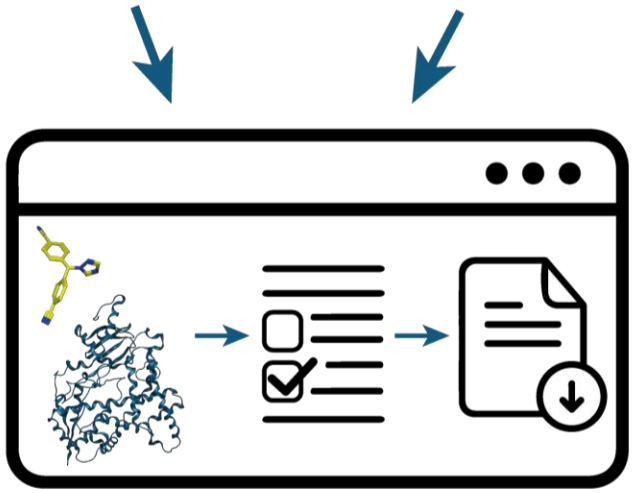
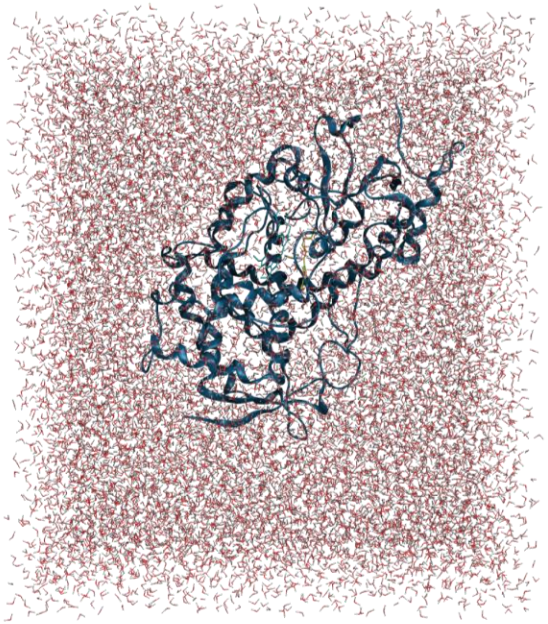


Structure-, System-
& simulation-configuration

Simulation



Preparation, Simulation
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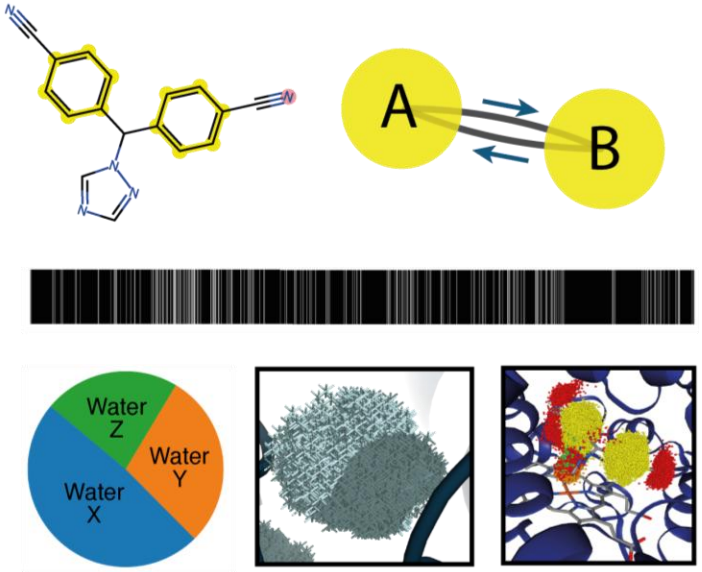
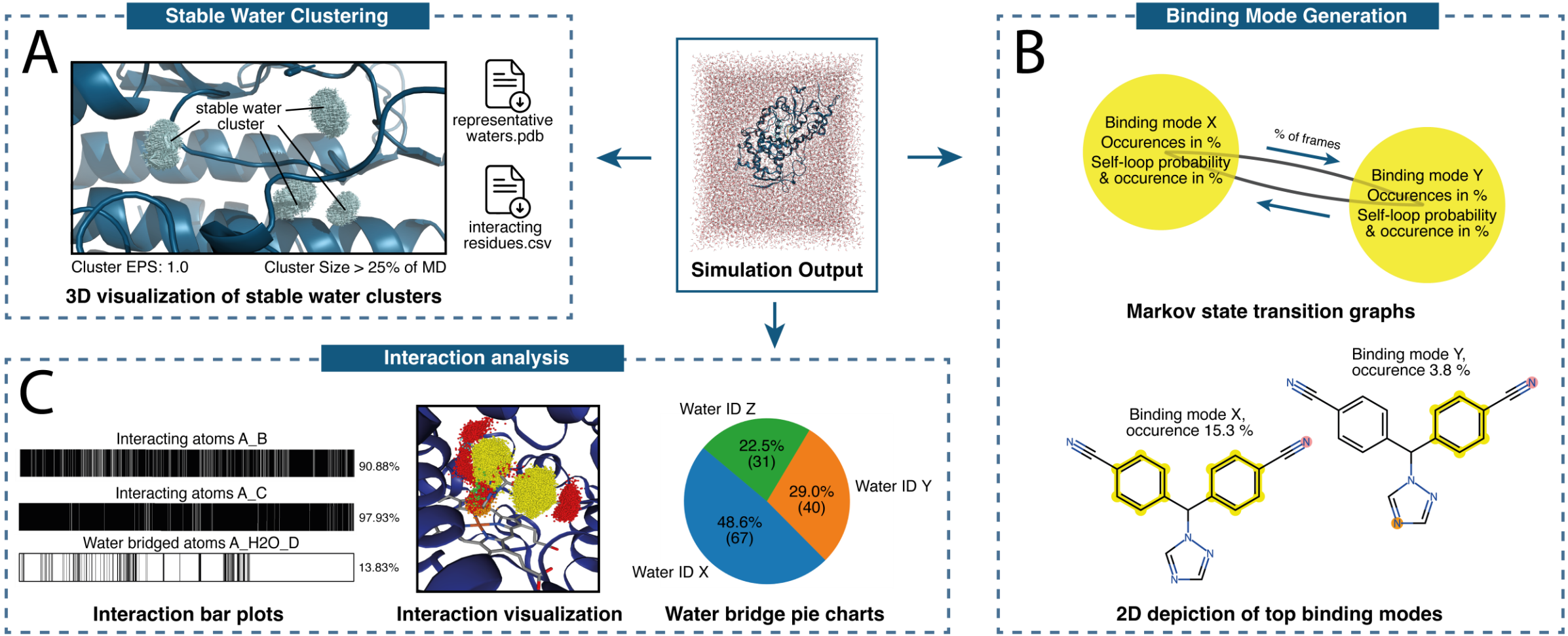
Analysis



Binding State Calculation,
Interaction Analysis,
& Water Bridge Calculation

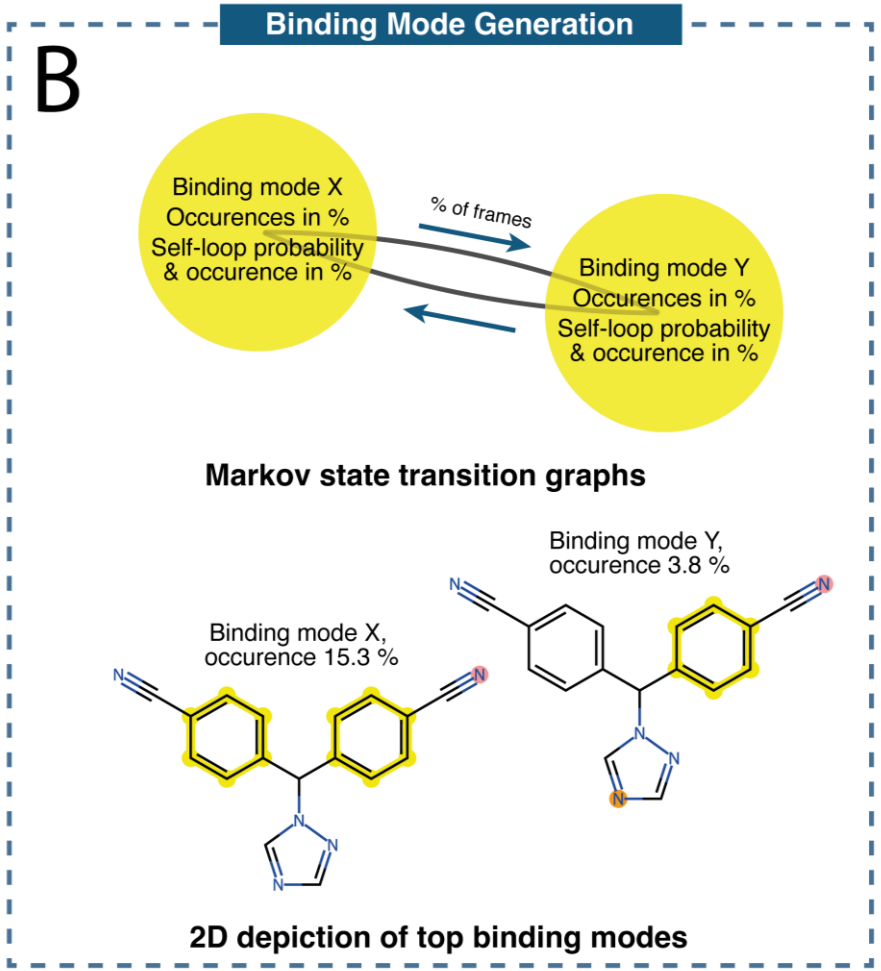
Analysis

- Analysis of MD simulation trajectory



Analysis

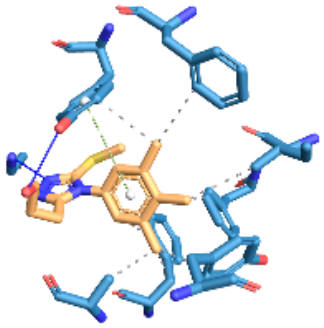
- Analysis of MD simulation trajectory
  - Stable water clustering:
    - Analysis of water movement
    - Creation of water clusters
  - Binding mode generation:
    - PLIP for protein-ligand interaction recognition
      - Implementation of ProLIF



Analysis

- PLIP (Protein-Ligand Interaction Profiler):
  - Webserver
  - Python package

Interacting chains: A, B



Protein
Ligand
Water
Charge Center
Aromatic Ring Center
Metal Ion
Hydrophobic Interaction
Hydrogen Bond
Water Bridge
π-Stacking (parallel)
π-Stacking (perpendicular)
π-Cation Interaction
Halogen Bond
Salt Bridge
Metal Complexation

Click for 3D-View

Download visualization in PyMol format (.pse)

Download visualization as image (.png)

Hydrophobic Interactions

Index	Residue	AA	Distance	Ligand Atom	Protein Atom
1	346A	PHE	3.83	12172	2419
2	348A	TYR	3.61	12172	2440
3	403A	ILE	3.76	12173	2893
4	405A	PHE	3.85	12159	2912
5	494B	PHE	3.87	12157	9409
6	494B	PHE	3.74	12175	9406
7	518B	ALA	3.57	12175	9591
8	567B	TYR	3.98	12175	9978

Hydrogen Bonds

Index	Residue	AA	Distance H-A	Distance D-A	Donor Angle	Protein donor?	Side chain	Donor Atom	Acceptor Atom
1	348A	TYR	3.01	3.48	111.30	×	✓	12162 [O3]	2443 [O3]
2	351A	GLY	1.79	2.75	165.76	✓	×	2461 [Nam]	12169 [Nar]

π-Stacking

Index	Residue	AA	Distance	Angle	Offset	Stacking Type	Ligand Atoms
1	348A	TYR	5.02	69.93	1.08	T	12157, 12158, 12159, 12161, 12171, 12174

Analysis

- ProLIF (Protein-Ligand Interaction Fingerprints):
  - Python package
  - Waterbridge interaction implementation
- MDAnalysis / Google Summer of Code
  - H-Bond Interactions from Implicit Hydrogens
  - Enhancing ProLIF Visualizations

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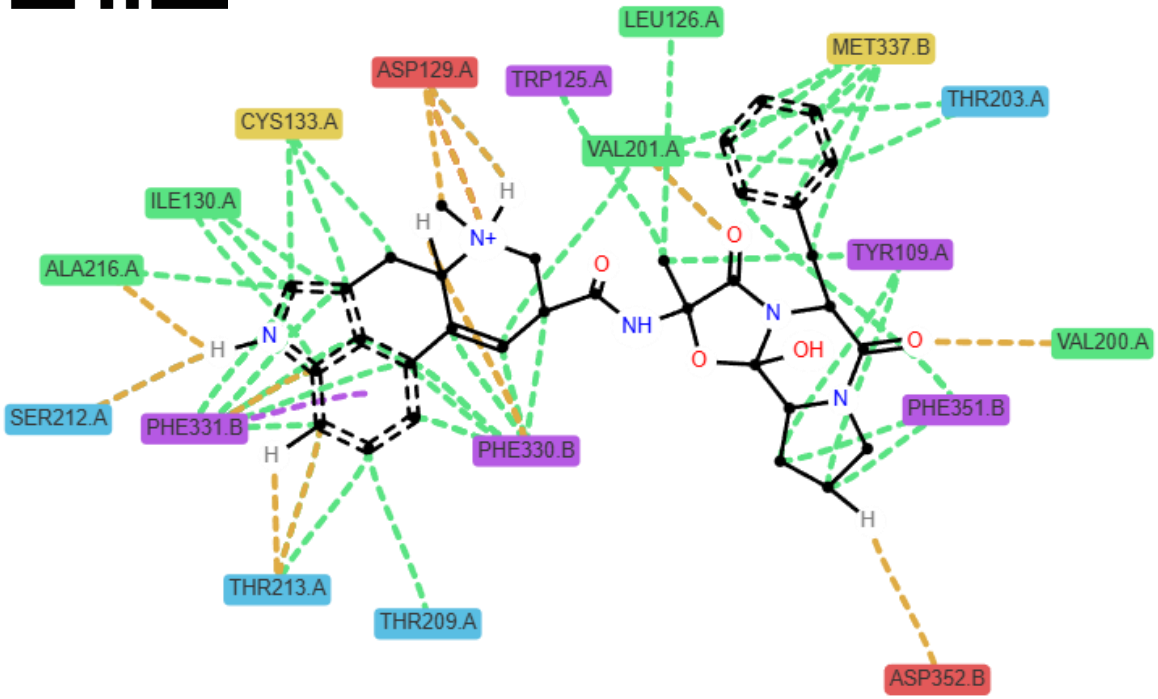
Yu-Yuan (Stuart) Yang

Nilay Verma



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Thank you for your attention!

OpenMMDL

ProLIF