multiSMD Manual

A Python toolkit for multi-directional Steered Molecular Dynamics simulations

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1. Introduction

multiSMD is a Python-based toolkit designed to automate multi-directional Steered Molecular Dynamics (SMD) simulations in NAMD and GROMACS. It systematically probes mechanical anisotropy in biomolecular systems by:

- Generating pulling vectors covering a hemispherical space (default: 9 directions)
- Preparing complete input files for SMD simulations
- Providing analysis tools for force profiles and structural changes

Key applications include:

- Studying direction-dependent protein-protein/ligand interactions
- Investigating mechanical stability of molecular complexes
- Analyzing unbinding pathways and energy landscapes

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2. Installation

Requirements:

- Python 3.x
- MDAnalysis

- NumPy
- SciPy

Installation:

```bash
pip install numpy scipy MDAnalysis
```

or via conda:

```bash
conda install numpy scipy MDAnalysis
```

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3. Quick Start

For NAMD:

```bash
python multiSMD.py system.pdb system.psf restart.vel restart.coor restart.xsc toppar.zip template.inp template.run 'segid A and name CA' 'segid B and name CA'
```

For GROMACS:

```bash
python multiSMD_GRO.py system.pdb system.gro restart_md.zip template.mdp 'segid A and name CA' 'segid B and name CA' 3
```

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4. Detailed Usage

4.1 NAMD Version

Required Parameters:

Parameter	**Description**
`file.pdb`	System structure in PDB format
`file.psf`	PSF topology file
`file.vel`	Velocity restart file

`file.coor`	Coordinate restart file
`file.xsc`	Periodic cell parameters
`toppar.zip`	CHARMM force field parameters
`template.inp`	NAMD configuration template
`template.run`	Job submission script template
`'selection constraints'`	MDAnalysis selection syntax for fixed atoms
`'selection pull'`	MDAnalysis selection syntax for pulled atoms

Example:

```bash
python multiSMD.py complex.pdb complex.psf eq.vel eq.coor eq.xsc charmm36.zip smd_template.inp cluster_run.sh 'segid PROT and name CA' 'segid LIG and name C1 C2'
```

4.2 GROMACS Version

Required Parameters:

Parameter	**Description**
`file.pdb`	System structure (for chain info)
`file.gro`	GROMACS structure file
`restart_md.zip`	All simulation restart files
`template.mdp`	GROMACS mdp template
`'selection constraints'`	Fixed atoms selection
`'selection pull'`	Pulled atoms selection

`n_repeats`	Number of replicas per direction

Example:

```bash
python multiSMD_GRO.py complex.pdb eq.gro restart_files.zip smd.mdp 'chain A and name CA' 'resname LIG and name C*' 5
```

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5. Output Analysis

Analysis Scripts:

- NAMD: `Analysis.py`

  ```bash
  python Analysis.py Output/ 'segid A' 'segid B' 5
  ```

- GROMACS: `Analysis_GRO.py`

  ```bash
  python Analysis_GRO.py Output/ 'chain A' 'resname LIG' 5 complex.pdb
  ```

Output Metrics:

1. Force vs. time profiles
2. Force vs. distance plots
3. Hydrogen bond dynamics
4. Maximum rupture forces

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6. Visualization

The toolkit generates:

- `vmd_script.tcl` for visualizing pulling vectors in VMD
- Matplotlib plots of analysis results

Example VMD visualization:

```tcl
source vmd_script.tcl
```

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7. Case Studies

Demonstrated Applications:

1. SARS-CoV-2 Spike-ACE2 Complex
   - Anisotropic mechanical stability
   - Mutation effects on binding strength
2. Kir6.1/Kir6.2 Channels (Supplementary)
   - Isoform-specific ATP binding mechanics
3. SUR2B-KNt System (Supplementary)
   - Direction-dependent release of disordered regions
