

Supplementary Information

Preliminary Short-Timescale Solvent-Relaxation Analysis of KIF11–CHEMBL195232

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Supplementary Methods

All-atom molecular dynamics relaxation of the KIF11–CHEMBL195232 complex was conducted using GROMACS 2024 under the AMBER99SB-ILDN force field and GAFF/ACPYPE for ligand parameters. The complex was immersed in a TIP3P water box, neutralized with 0.15 M NaCl, energy-minimized, and equilibrated under NVT and NPT ensembles for 100 ps each at 300 K and 1 bar. A 1 ns production relaxation run was collected with a 2 fs time step. CHEMBL195232 was selected from the broader 20-compound docking panel as a representative complex before the final integrated lead ranking; the trajectory analysis was independent of QSAR model development, locked external validation, docking selection, and final lead ranking.

The analyzed trajectory corresponds to the actual 1 ns simulation segment. The source trajectory contained 500,000 integration steps with a 0.002 ps time step, corresponding to 1000 ps (1 ns); no temporal rescaling was applied. Trajectory-derived parameters included backbone RMSD, C α -fitted RMSD, residue-level RMSF, radius of gyration (R_g), solvent-accessible surface area (SASA), temperature, pressure, density, and potential energy.

Supplementary Table S1. Trajectory-derived structural and system-level parameters

Parameter	Mean	Minimum	Maximum	Terminal/peak
Backbone RMSD (nm)	0.1174	0.0005	0.1552	0.1244
C α RMSD (nm)	0.1668	0.0005	0.2012	0.1783
RMSF (nm)	0.0779	0.0374	0.3282	0.3282 ^a
Radius of gyration (nm)	2.0728	2.0413	2.1009	2.0701
SASA (nm ²)	175.60	163.60	181.06	173.51
Temperature (K)	300.06	295.62	303.50	299.17
Density (kg m ⁻³)	1007.06	992.03	1022.08	1005.26
Pressure (bar)	0.95	-412.53	433.29	60.04
Potential energy (kJ mol ⁻¹)	-850360.99	-854491.94	-846765.00	-851163.38

^aThe RMSF entry reports the peak residue-level fluctuation rather than a terminal time-point value; the peak occurred at residue 251. The analyzed trajectory segment covered 1 ns of simulation time.

Supplementary Results

The backbone RMSD showed an initial structural adjustment followed by comparatively restricted fluctuations over the analyzed segment. The mean backbone RMSD was 0.1174 nm, while the mean radius of gyration was 2.0728 nm. Residue-level fluctuations were highest at residue 251 (0.3282 nm). These observations describe the behavior of this particular short trajectory and are not interpreted as evidence of long-timescale complex stability or persistent ligand binding.

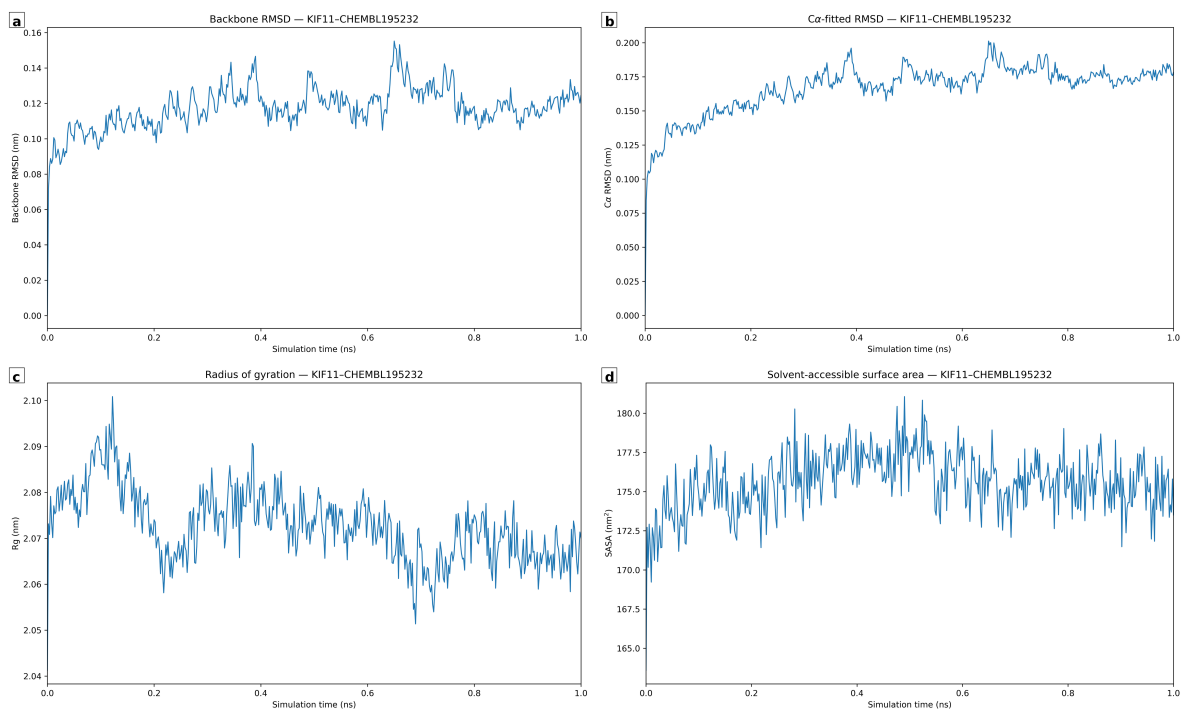


Figure 1: Supplementary Figure S1. Global structural parameters of the KIF11–CHEMBL195232 complex. Panels show backbone RMSD, $C\alpha$ -fitted RMSD, radius of gyration, and solvent-accessible surface area (SASA).

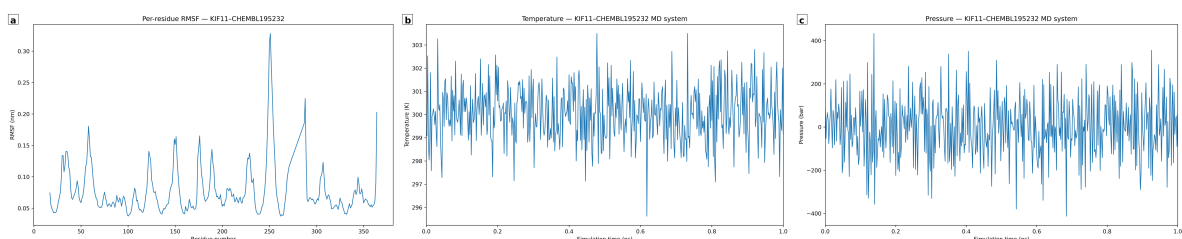


Figure 2: Supplementary Figure S2. Residue-level flexibility and system-level thermodynamic profiles. Panels show per-residue RMSF, temperature, and pressure for the KIF11–CHEMBL195232 trajectory.

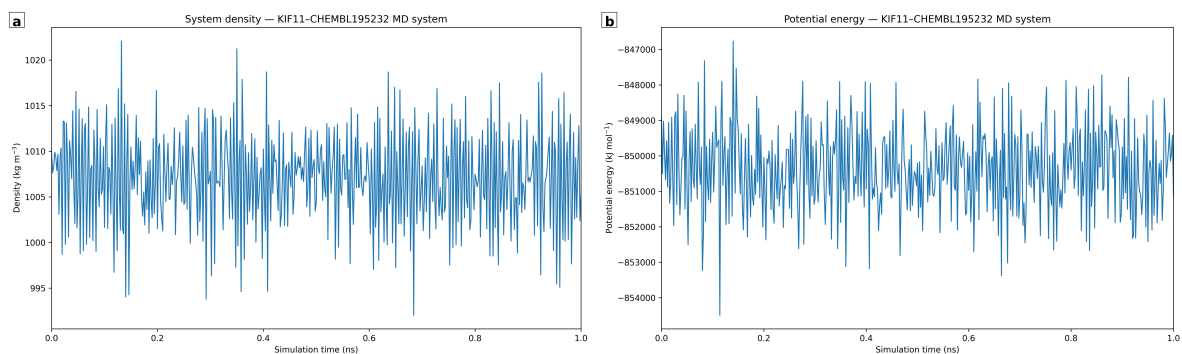


Figure 3: Supplementary Figure S3. Additional system-level trajectory variables showing density and potential energy for the KIF11–CHEMBL195232 system.