OxDC MD Simulations: Winter Break Updates

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1 Overview

- Completed 474 ns production run for BiOx+2 (bidentate oxalate, Mn(II))
- Ran full cpptraj analysis pipeline on production trajectory
- Generated analysis figures for structural stability, coordination, and lid dynamics
- Attempted equilibration of 1Wat+3 (Mn(III)), encountered numerical instability

2 BiOx+2 Production Run (474 ns)

2.1 Simulation Setup

Parameter	**Value**
System	BiOx+2 (bidentate oxalate, Mn(II), from 5VG3)
Total atoms	63,287 (19,079 TIP3P waters, 1 Cl^-)
Production length	474 ns (46,383 frames at 10 ps/frame)
GPU	NVIDIA B200 (hpg-b200), 467 ns/day

2.2 Structural Stability

The active site remained stable throughout the trajectory despite conformational sampling in flexible regions (N/C-termini):

Metric	**Backbone**	**Active Site**
Mean RMSD	4.70 ± 1.84 Å	1.77 ± 0.42 Å
Radius of gyration	24.02 ± 0.35 Å	

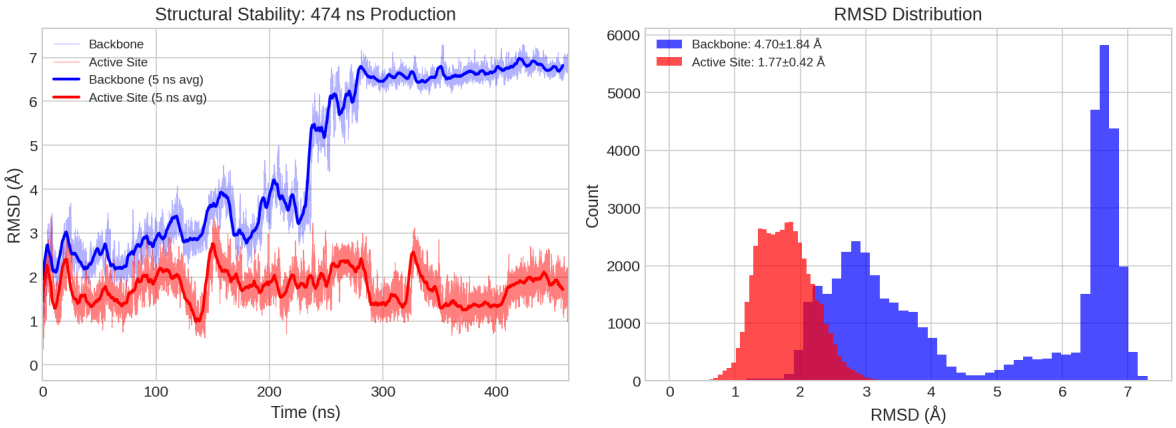

Figure 1: Backbone and active site RMSD over 474 ns. Higher backbone RMSD reflects terminal flexibility; active site remains stable.

2.3 Mn1 Coordination

All four protein ligands maintained coordination with zero dissociation events:

Ligand	Mean Distance (Å)	Dissociations
His95-NE2	2.42 ± 0.12	0
His97-NE2	2.27 ± 0.09	0
His140-NE2	2.22 ± 0.09	0
Glu101-OE1	2.06 ± 0.09	0

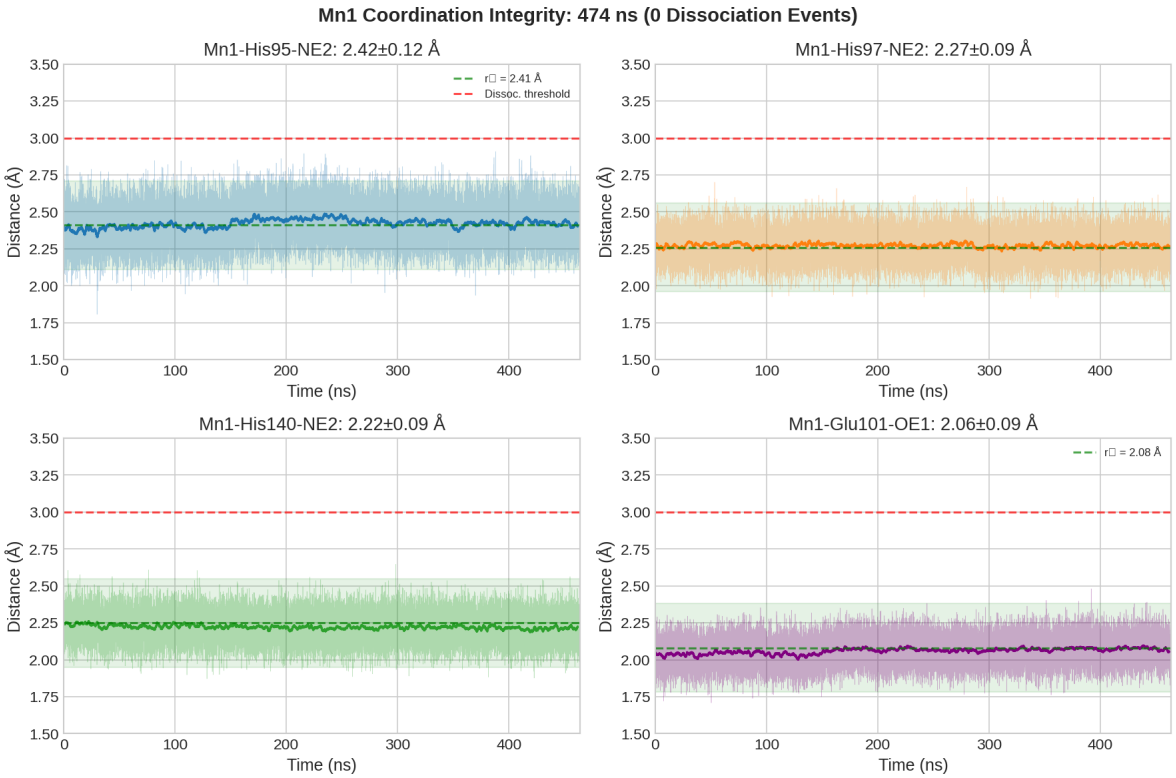

Figure 2: Mn1-ligand distances. Green shading = expected r_0 range; red dashed = 3.0 Å dissociation threshold.

2.4 Oxalate Binding

Oxalate maintained asymmetric bidentate coordination (92.6% of trajectory):

Oxygen	Mean Distance (Å)	Mode
OZ	2.09 ± 0.07	Tight
OX	2.35 ± 0.11	Loose

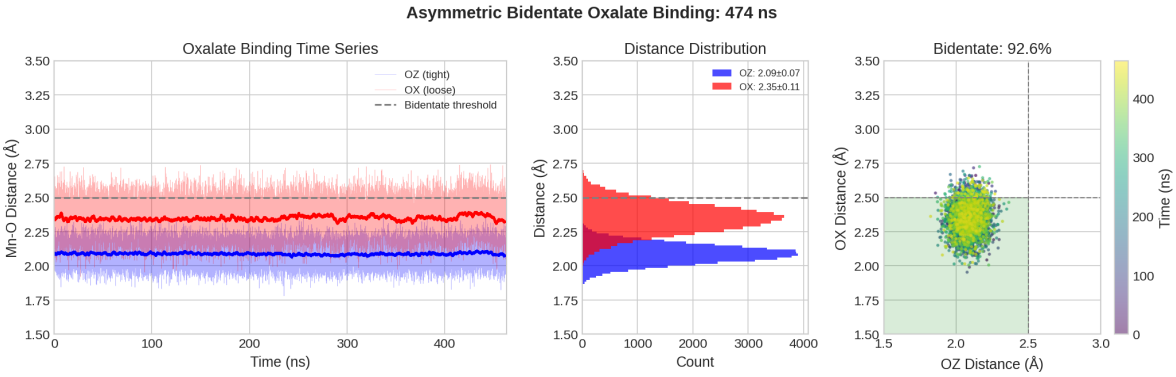

Figure 3: Oxalate binding analysis showing persistent asymmetric bidentate coordination.

2.5 Lid Dynamics

Flexible loop did not appear to change conformation during the simulation: the Glu162 sidechain remained in the 5VG3-like "closed-backbone / Glu162-out" position throughout the simulation. While doing this analysis ran into some confusion on the definitions of "closed" and "open" flexible loop states. For reference, compiled the three lid states from literature:

State	PDB	Glu162-Mn (Å)
Open-loop	1J58	∼15–16
Glu162-in (catalytic)	1UW8	∼4.6–5.1
Closed-backbone, Glu162-out	5VG3	∼10–12
This simulation	—	**12.0 ± 0.7**

No transitions toward the Glu162-in state were observed (closest approach: 8.23 Å at 229 ns). The lid region showed below-average flexibility (RMSF = 0.71 Å vs 1.03 Å global average), suggesting the Glu162-out conformation is stabilized in this system.

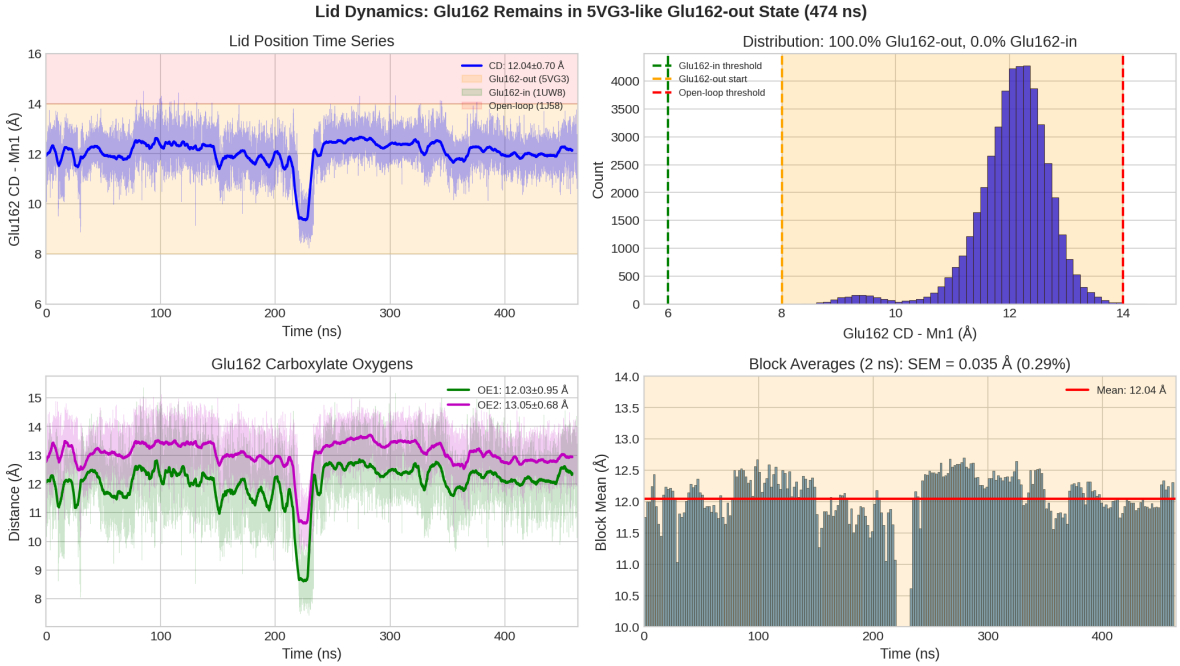

Figure 4: Glu162-Mn distance over 474 ns showing persistent Glu162-out state.

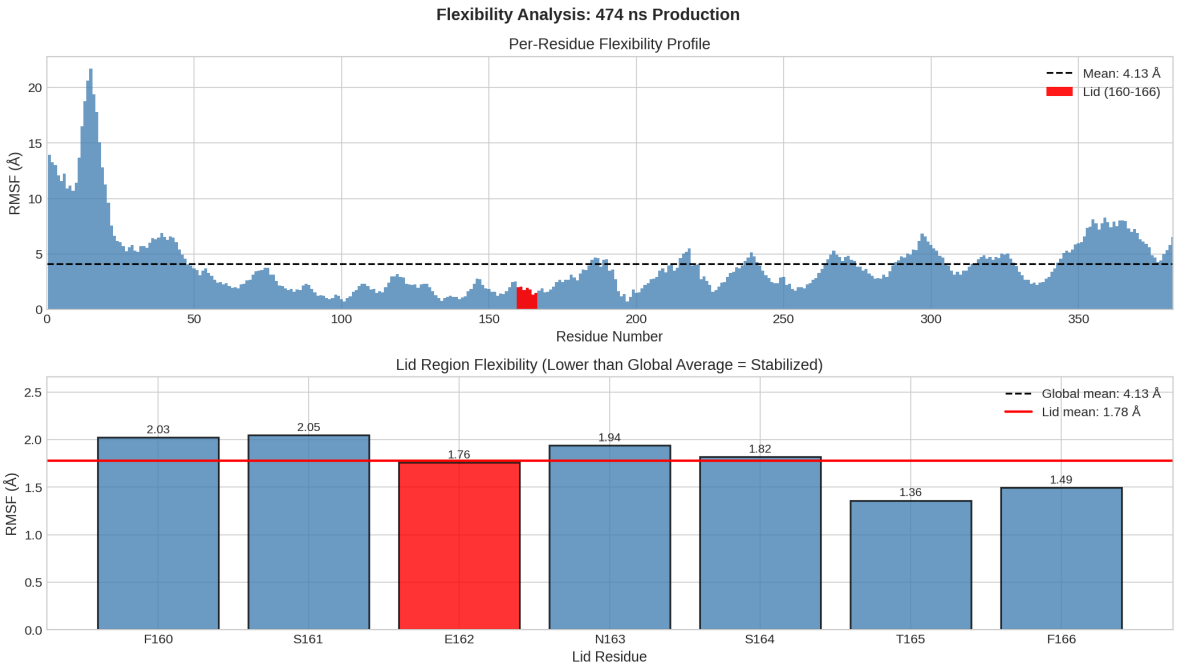

Figure 5: Per-residue RMSF. Lid region (160–166) highlighted.

2.6 Convergence

Block averaging (231 blocks × 2 ns) confirms good convergence:

Metric	Mean	SEM	SEM %
Backbone RMSD (Å)	4.70	0.120	2.56%
Active Site RMSD (Å)	1.77	0.024	1.35%
Glu162-Mn (Å)	12.04	0.035	0.29%

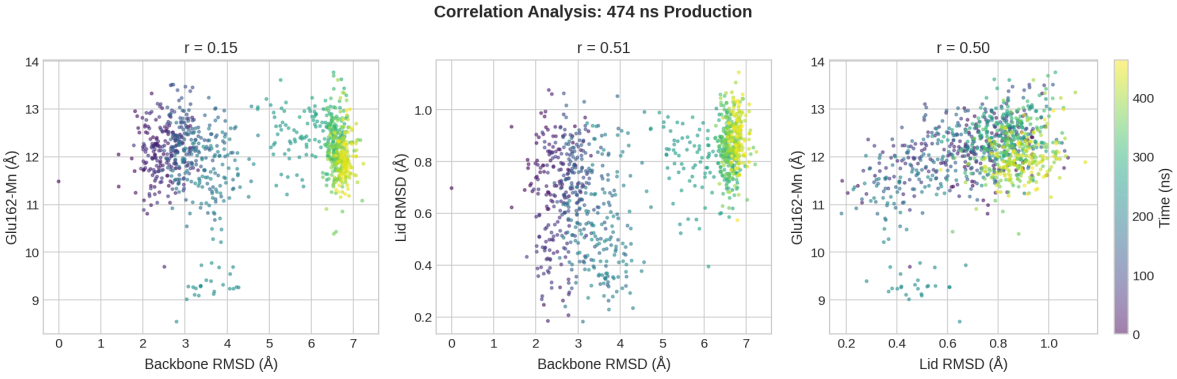

Figure 6: Correlation analysis between structural metrics.

3 1Wat+3 Equilibration (Mn(III))

The 1Wat+3 system (water-coordinated Mn(III)) was equilibrated but showed significant numerical instability:

Stage	vlimit Warnings	Status
heat.cpu	2,467	Completed
eq1.cpu	6,174	Completed
eq1a.cpu	2,127	Completed
eq1b.cpu	1,179	Completed
Total	**11,947**	—

The instability might stem from elevated Mn(III) force constants from MCPB.py (85–125 kcal/mol·Å^2 vs 29.7 for BiOx+2). Might reflect Jahn-Teller distortion that classical harmonic potentials struggle to represent. Production runs for 1Wat+3 might not be possible until parameterization is addressed, may require QM/MM.

4 Next Steps

1. **Extend production** — At 467 ns/day (on B200s), reaching 1 μs takes $\sim$2 days. Would help determine if Glu162-in is ever kinetically accessible from this state.
2. **Address 1Wat+3 parameterization** — Investigate Mn(III) parameters or investigate whether QM/MM is needed for Mn(III) systems.
3. **Enhanced sampling** — Metadynamics with Glu162-Mn as CV could estimate the free energy barrier for Glu162-out $\rightarrow$ Glu162-in transition.