**Table S3: Average change in binding affinities between the duplicate trajectories.** Energy for the metal-cofactor complex before and after the conformational shift (Δ*Gshift)*, average free energy of binding for the cofactor-metal complex (Δ*Gbinding),* average change in binding enthalpy for the metal-cofactor complex before and after the conformational shift (ΔH*shift*) and the average enthalpy of binding for the cofactor-metal complex (Δ*Hbinding*) between the duplicate trajectories. All energies are listed in kcal/mol.

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| Trajectory type | Δ*Gshift* | Δ*Gbinding\** | ΔH*shift*  | Δ*Hbinding* |
| Wild type  | 1.83±4.13 | 1.26±4.07 | 1.57±3.65 | -29.20±3.85 |
| Mutant | 29.75±3.30 | 30.21±2.60 | 31.37±2.60 | 0.73±3.07 |

\*These averages are taken subsequent to the conformational change (~100 ns) for the mutant trajectories.