Electronic Supplementary Material (ESI) for Metallomics.

Supporting information for: Destabilization of the metal site as a hub for the pathogenic mechanism of five ALS-linked mutants of copper, zinc superoxide dismutase

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Tomasz Bereźniak, and Christian Ochsenfeld

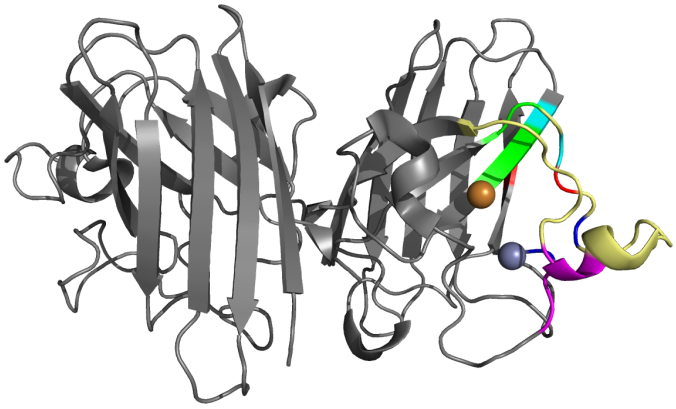


Figure 1: Crystallographic structure of the reduced form of SOD1. The electrostatic loop is depicted in pale yellow. Interaction sites between the electrostatic loop and other structural elements of the protein are depicted in colors.

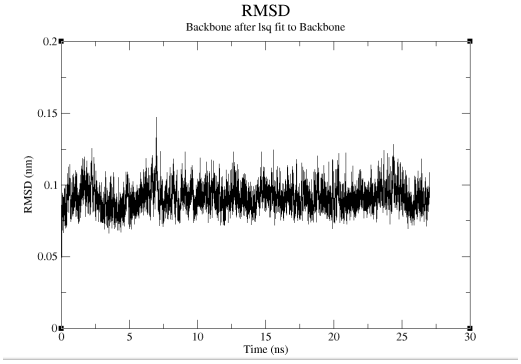


Figure 2: RMSD for the backbone of the first MD trajectory for the wild-type variant of SOD1.

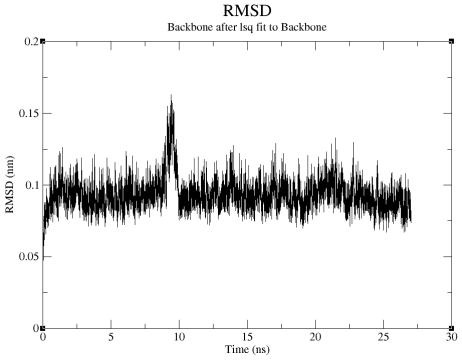


Figure 3: RMSD for the backbone of the second MD trajectory for the wild-type variant of SOD1.

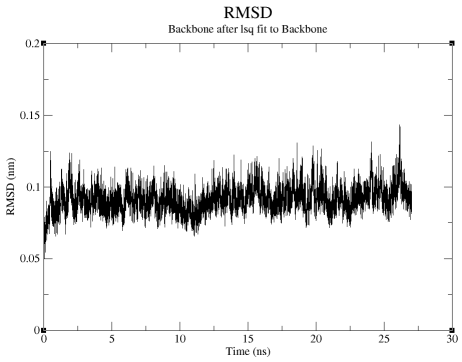


Figure 4: RMSD for the backbone of the third MD trajectory for the wild-type variant of SOD1.

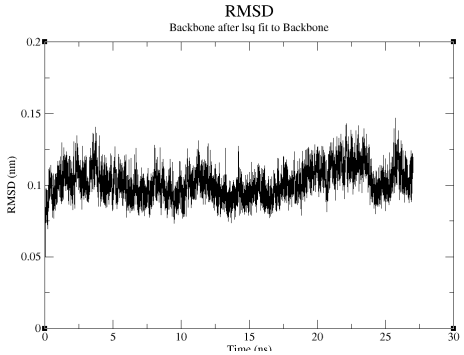


Figure 5: RMSD for the backbone of the first MD trajectory for the L126S mutant variant of SOD1.

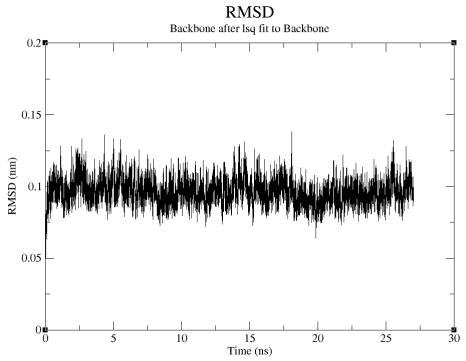


Figure 6: RMSD for the backbone of the second MD trajectory for the L126S mutant variant of SOD1.

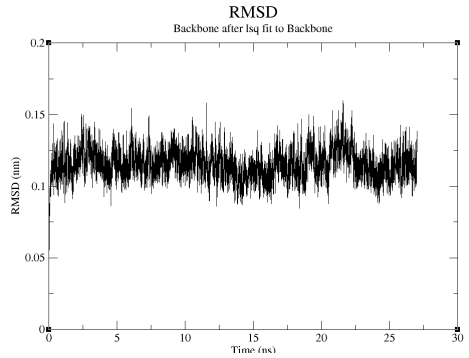


Figure 7: RMSD for the backbone of the third MD trajectory for the L126S mutant variant of SOD1 (which is also shown in Figure 7 of the article).

Table 1: The dissociation events for the D124–H46 interaction in MD trajectories for the wild-type (WT) and mutant (L126S) variants of SOD1. Only events longer than 1 ps are shown. Each number corresponds to the duration of the corresponding event, in ps.

Trajectory	Dissociation events longer than 1 ps.
WT-1	2
WT-2	–
WT-3	–
L126S-1	3, 18, 15, 5, 2, 40, 14, 79, 15, 11, 14, 43, 8, 113, 12, 3, 3, 2, 1, 9, 16,13
L126S-2	2, 2, 2, 3, 16, 2, 11, 2, 2, 6, 46, 49, 20, 3, 20, 5, 5, 3, 26
L126S-3	18, 47, 5, 18, 30, 3, 11, 4, 6, 2, 2, 43, 9, 14, 7, 16, 34,2, 12, 59, 13, 29, 13, 2, 11, 87, 15, 32, 10, 76, 64, 63, 10, 2, 42

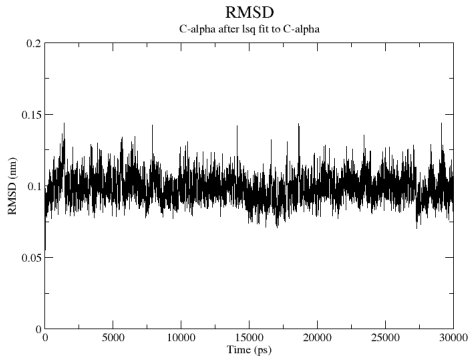


Figure 8: RMSD for the backbone of the first MD trajectory for the N86K mutant variant of SOD1.

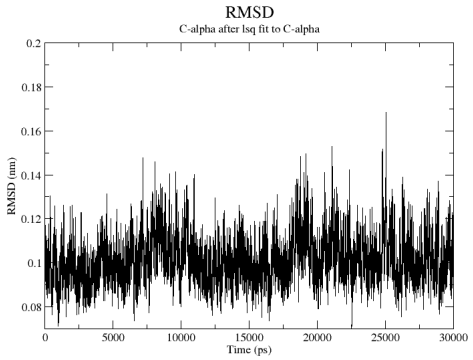


Figure 9: RMSD for the backbone of the second MD trajectory for the N86K mutant variant of SOD1.

Table 2: Interaction energies at the BLYP-D3/def2-TZVPP level of theory for different-sized reduced models of the N86K mutant version of the contact point 1.

Reduced model	Number of atoms	E (kcal/mol)
V1 (original)	35	−6.1
V2	111	−4.5
V3	124	−7.2

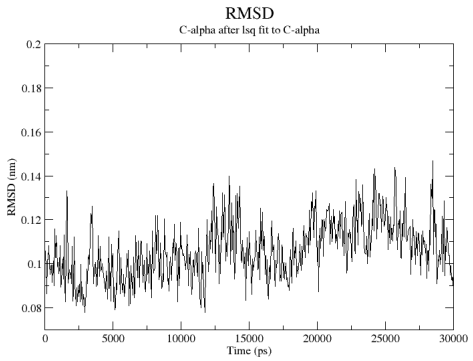
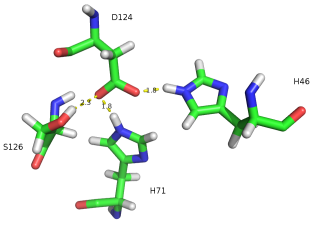
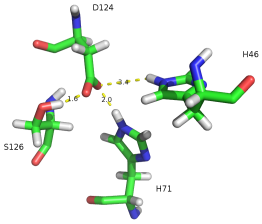


Figure 10: RMSD for the backbone of the third MD trajectory for the N86K mutant variant of SOD1.



(a) O ns



(b) $\sim$ 12 ns

Figure 11: The residues H46, H71, D124 and S126 in the third MD trajectory for the L126S mutant of SOD1 at

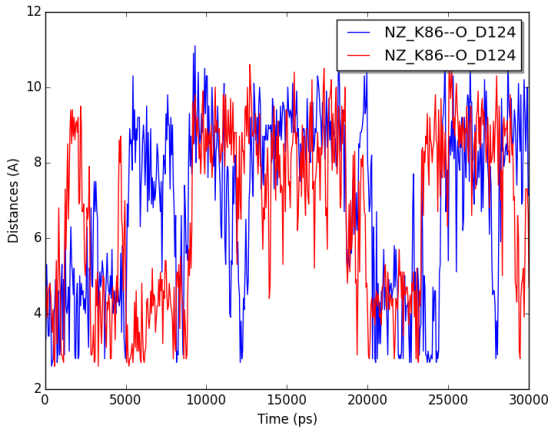


Figure 12: Distances for the interaction between the ζ-nitrogen of K86 and the backbone oxygen of D124 along the first trajectory for the N86K mutant structure. The distances are shown in blue and red for each monomer of the protein. Atoms are labeled following the PDB convention.

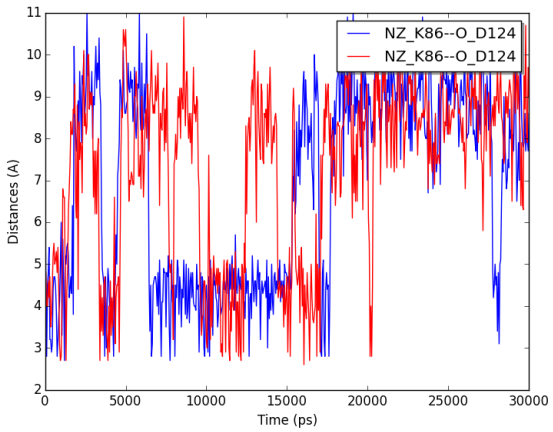


Figure 13: Distances for the interaction between the ζ-nitrogen of K86 and the backbone oxygen of D124 along the third trajectory for the N86K mutant. The distances are shown in blue and red for each monomer of the protein. Atoms are labeled following the PDB convention.

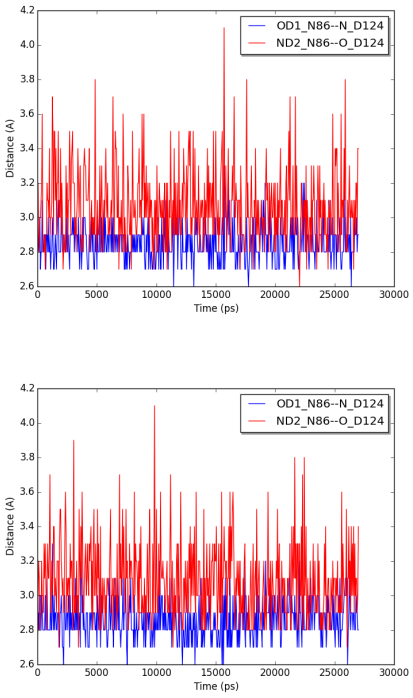


Figure 14: Distances for the interaction between the δ_1 oxygen and δ_2 nitrogen of N86 and the backbone nitrogen and oxygen of D124, in blue and red, respectively, along the first trajectory for the WT structure. Both monomers are shown. Atoms are labeled following the PDB convention.

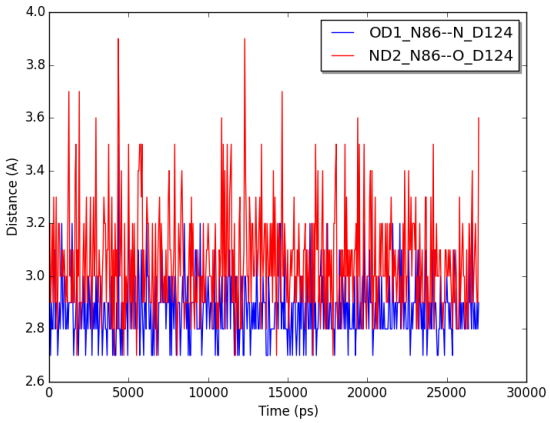


Figure 15: Distances for the interaction between the δ_1 oxygen and δ_2 nitrogen of N86 and the backbone nitrogen and oxygen of D124, in blue and red, respectively, along the second for the WT structure. One monomer is shown (the other is shown in the Figure 9 of the article). Atoms are labeled following the PDB convention.

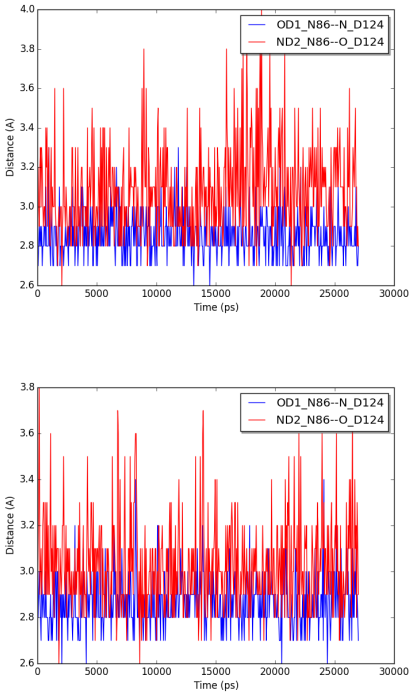


Figure 16: Distances for the interaction between the δ_1 oxygen and δ_2 nitrogen of N86 and the backbone nitrogen and oxygen of D124, in blue and red, respectively, along the third trajectory for the WT structure. Both monomers are shown. Atoms are labeled following the PDB convention.

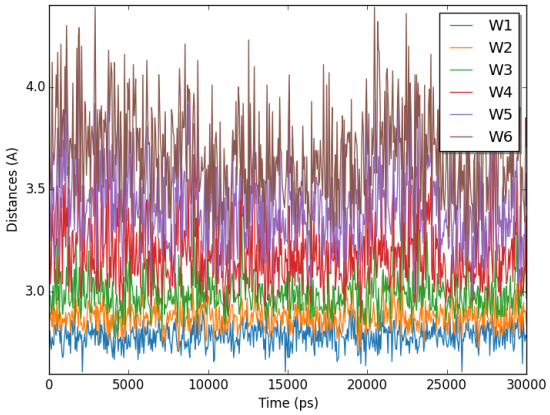


Figure 17: Distances for the six closest water to the terminal nitrogen of K86 along the first trajectory for the N86K mutant structure. The waters molecules are not necessarily the same for each point in the trajectory. Distances are averaged for both monomers.

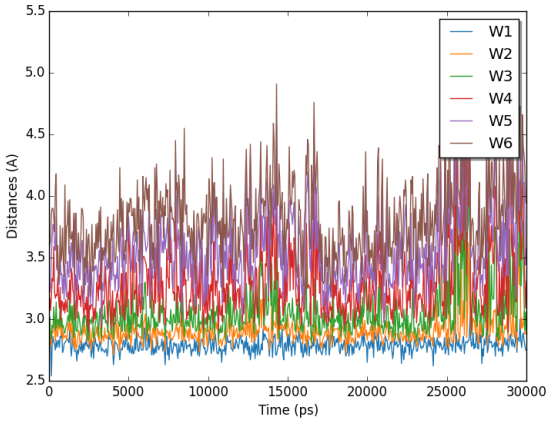


Figure 18: Distances for the six closest water to the terminal nitrogen of K86 along the second trajectory for the N86K mutant structure. The waters molecules are not necessarily the same for each point in the trajectory. Distances are averaged for both monomers.

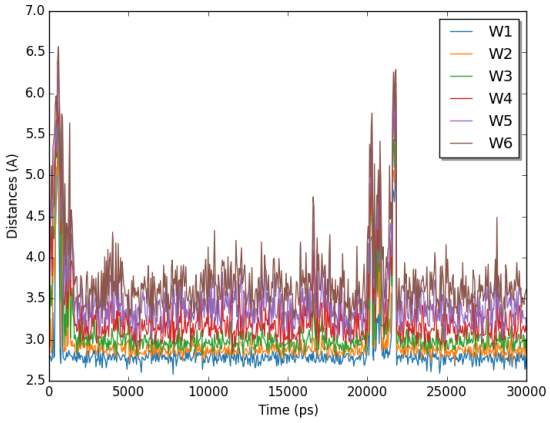
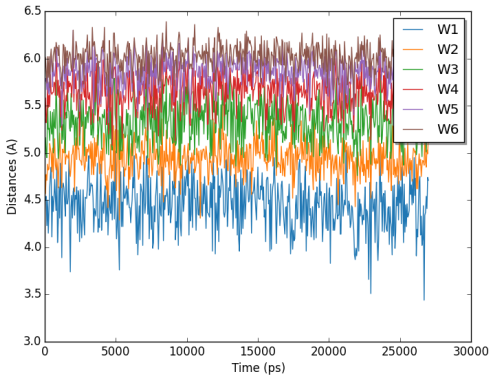
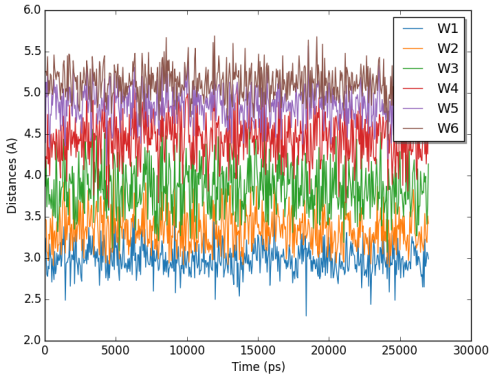


Figure 19: Distances for the six closest water to the terminal nitrogen of K86 along the third trajectory for the N86K mutant structure. The waters molecules are not necessarily the same for each point in the trajectory. Distances are averaged for both monomers.

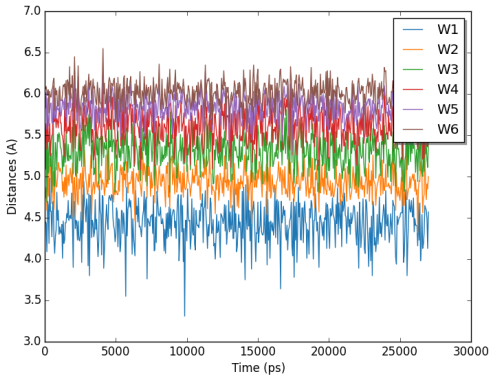


(a) $O_{\delta 1}$

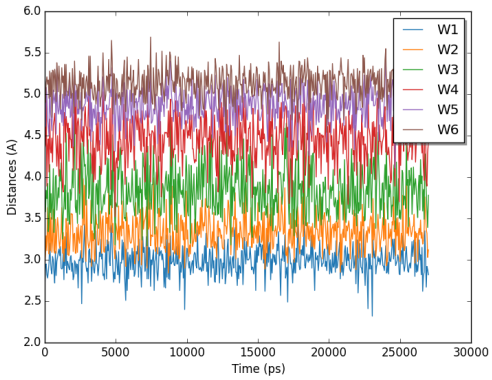


(b) $N_{\delta 2}$

Figure 20: Distances for the six closest waters to the δ_1 oxygen and δ_2 nitrogen of N86, along the first trajectory for the WT structure. The waters molecules are not necessarily the same for each point in the trajectory. Distances are averaged for both monomers.

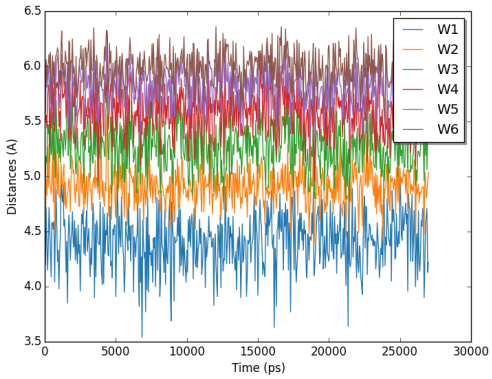


(a) $O_{\delta 1}$

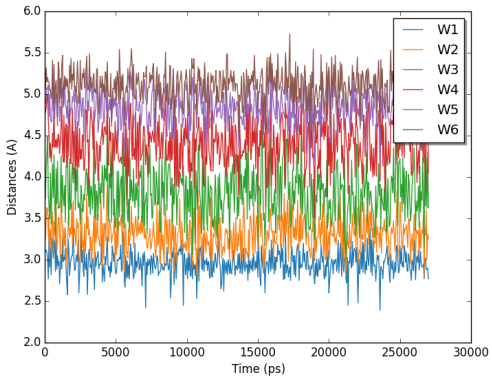


(b) $N_{\delta 2}$

Figure 21: Distances for the six closest waters to the δ_1 oxygen and δ_2 nitrogen of N86, along the second trajectory for the WT structure. The waters molecules are not necessarily the same for each point in the trajectory. Distances are averaged for both monomers.



(a) $O_{\delta 1}$



(b) $N_{\delta 2}$

Figure 22: Distances for the six closest waters to the δ_1 oxygen and δ_2 nitrogen of N86, along the third trajectory for the WT structure. The waters molecules are not necessarily the same for each point in the trajectory. Distances are averaged for both monomers.