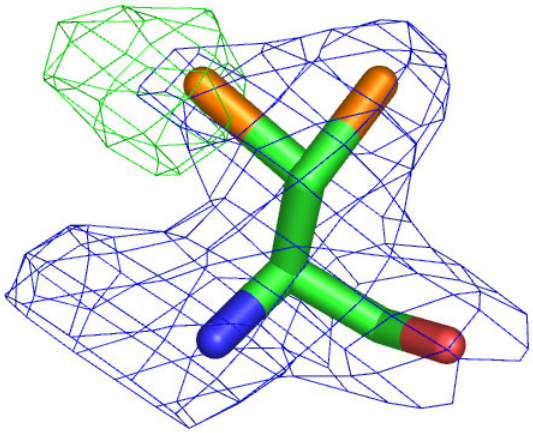
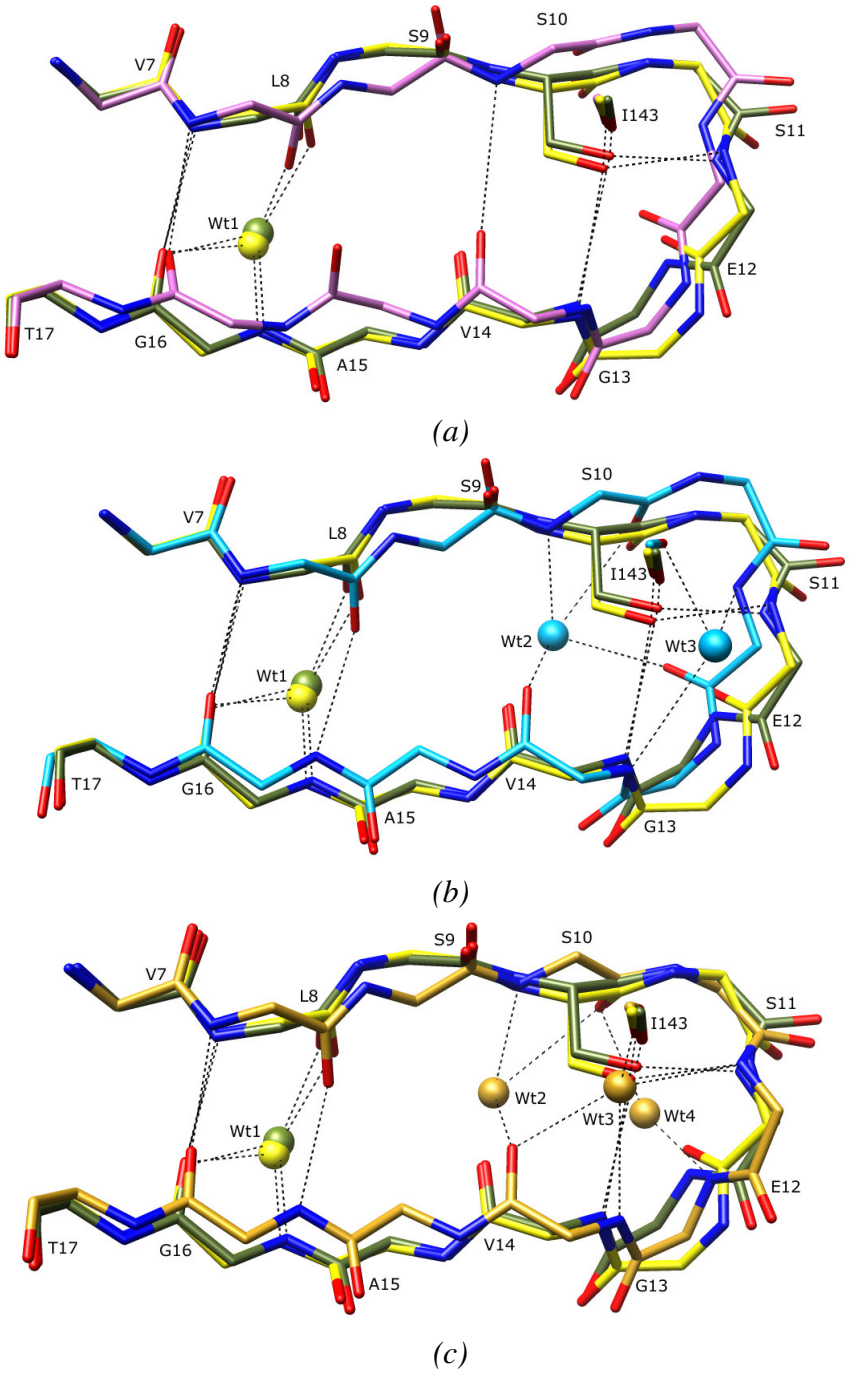
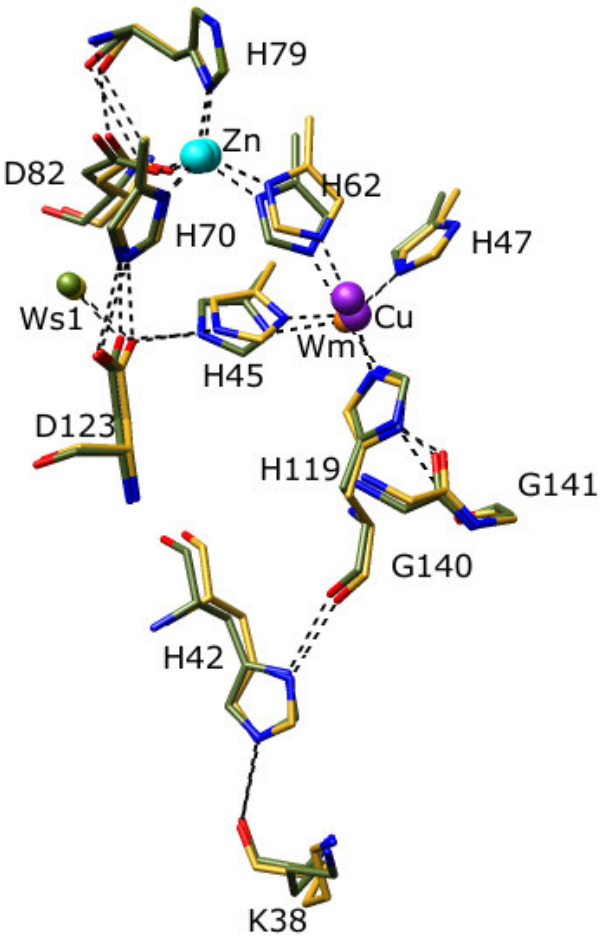


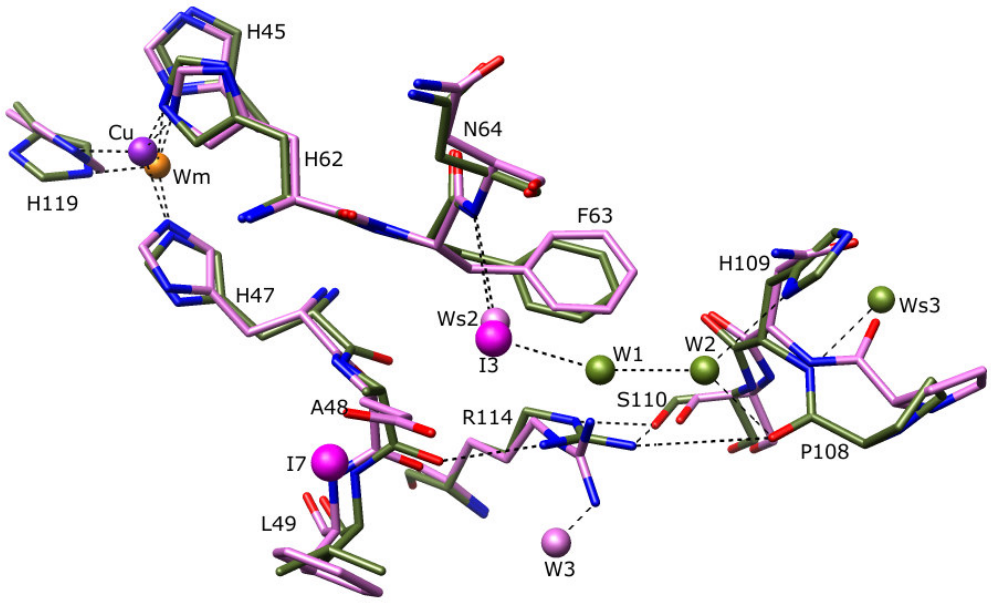
Supplementary Figure S1. Alternate conformation of the free Cys95 in molecule B of Pa-SOD. Electron density maps ($2F_o$-F_c) and (F_o-F_c) are contoured at 1.2σ and 3σ level respectively.



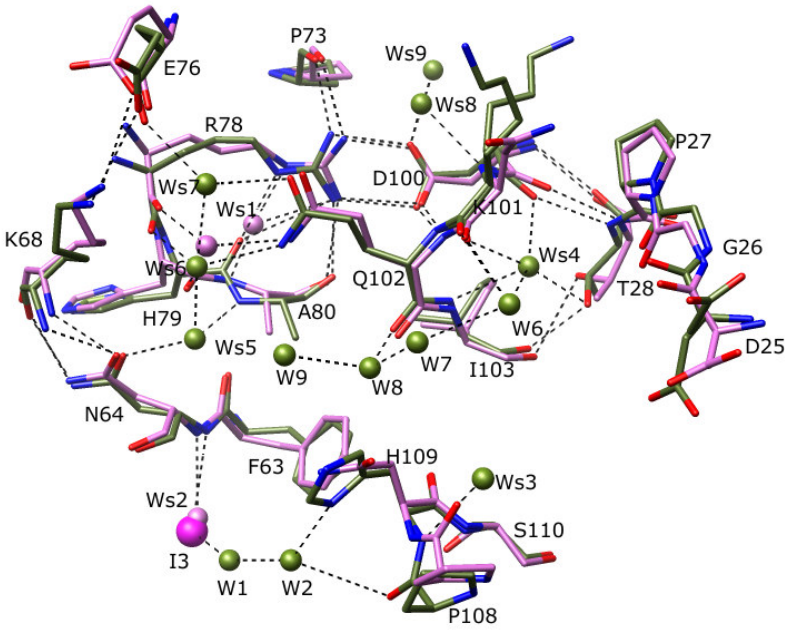
Supplementary Figure S2. Comparison of loop I structure of eukaryotic CuZnSODs. *(a)* Molecules A (Olive green) and B (Yellow) of Pa-SOD with So-SOD (Orchid), *(b)* Pa-SOD with Hs-SOD (Deep sky blue). The loop I structure in Sc, Sm, Bt and Xl-SODs is the same as in Hs-SOD. *(c)* In Sc and Sm-SODs (Gold) an additional water molecule Wt4 is present. For clarity, side-chains are not shown except for Ser10 in Pa-SOD and the residues are labeled according to Pa-SOD numbering.



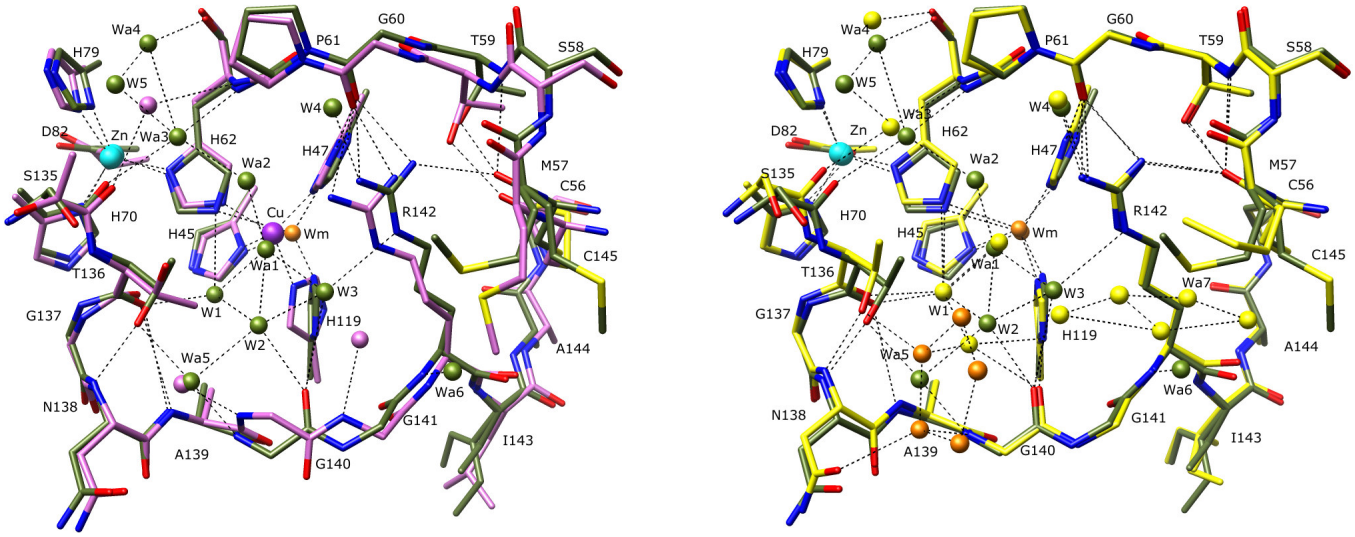
Supplementary Figure S3. Comparison of metal binding residues with secondary shell stabilization residues of Pa-SOD (Olive green) and Sm-SOD (Gold). The water molecule Wm (orange) in Pa-SOD superimposes with the higher occupancy copper site of Sm-SOD.



Supplementary Figure S4. Comparison of water Ws2 and Arg114 of copper unbound Pa-SOD and the early bound state So-SOD.

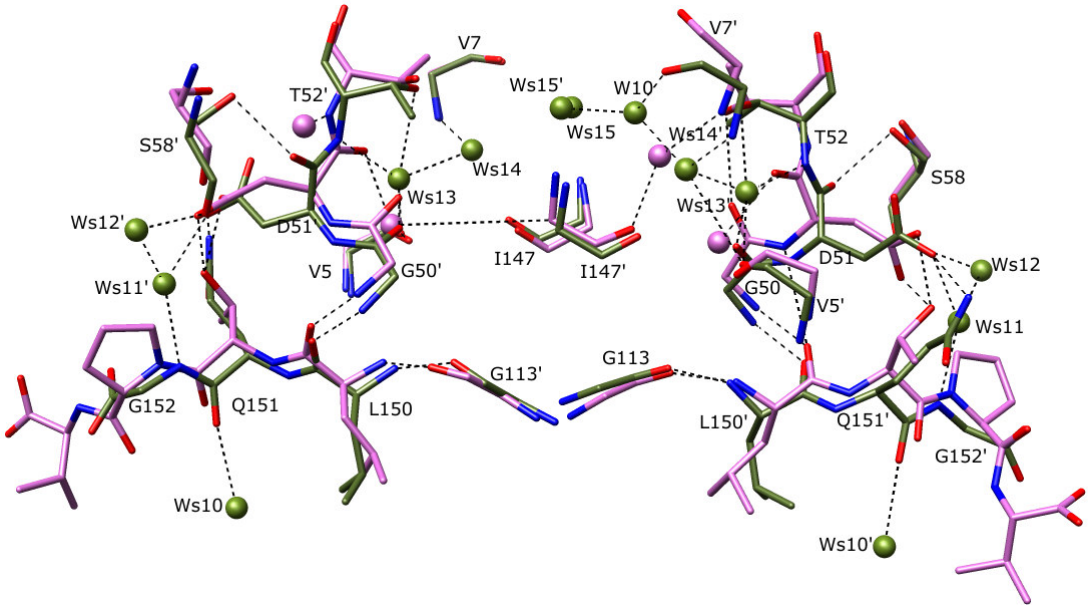


Supplementary Figure S5. Movements of the structural water and the C-terminal Greek key loop between copper unbound Pa-SOD (Olive green) and the early copper bound state So-SOD (Orchid).



(a) *(b)*

Supplementary Figure S6. Comparison of active site water molecules of copper unbound Pa-SOD with early chelation state So-SOD. Views of *(a)* Superposition of Cu unbound Pa-SOD (Olive green) and the early copper bound state So-SOD (Orchid) and *(d)* Superposition of molecules A and B of Pa-SOD. Additional five-membered ring water structures are observed for molecule B of Pa-SOD.



Supplementary Figure S7. Comparison of dimeric interfaces of Pa-SOD (Olive green) and So-SOD (Orchid).

Conserved secondary shell interactions in solution and crystal structures of CuZnSODs

(i) backbone N of His62 with carbonyl O of 135 (Lys/Ser/Thr/Val)

(ii) backbone N of His70 and carbonyl O of 134 (Lys/Leu/Thr/Pro)

(iii) backbone N of His79 with the side chain $O^{\delta 2}$ of Asp82

(iv) backbone N of Asp82 with carbonyl O of His79

(v) backbone N of His119 and carbonyl O of Gly43

(vi) carbonyl O of His119 with $N^{\delta 1}$ of His42 [except Sc-SOD where His is replaced by Arg (Djinović *et al.*, 1992)]

(vii) carbonyl O of His79 also with N^{ε} of Arg78

(viii) carbonyl O of His62 with water molecule

(ix) carbonyl O of His70 with water molecule

(x) $N^{\varepsilon 2}$ of His45 with side chain $O^{\delta 1}$ or $O^{\delta 2}$ of Asp123

(xi) $N^{\delta 1}$ of His119 with carbonyl O of Gly140

(xii) $N^{\varepsilon 2}$ of His70 with side chain $O^{\delta 1}$ and $O^{\delta 2}$ of Asp123

(xiii) $N^{\delta 1}$ of His47 with carbonyl O of Gly60

(xiv) $N^{\varepsilon 2}$ of His79 with carbonyl O of 68 (Lys/Arg/Gln) through water molecule.

(xv) Residues His45 and His47 are part of β-strand *4f* and interact with residues Val117 and Ala/Ser/Thr115 in the β-strand *7g*. A slight movement in the carbonyl O of His47 is found for most of the SOD structures studied so far and thus, the distance between carbonyl O of His47 with N of 115 is >3.0 Å for all the structures.

Supplementary Table 1. Conserved hydrogen bonding interactions in the zinc binding loop

1. Salt Bride		
i.	Arg78	Asp100
	$N^{\eta 1}$ Arg78	$O^{\delta 1}$ Asp100
	$N^{\eta 2}$ Arg78	$O^{\delta 2}$ Asp100
2. Main-chain - main-chain interaction		
i.	N (Gly/Ser/Asn/Lys)67	O Asn64
ii.	N Gly81	O Phe63
iii.	N Asp82	O His79
3. Main-chain - side-chain interaction		
i.	N Gly71	$O^{\delta 2}$ Asp82
ii.	N (Lys/Arg/Gln)68	$O^{\delta 1}$ Asn64
iii.	O (Lys/Arg/Gln)68	$N^{\delta 2}$ Asn64
iv.	O His79	N^{ε} Arg78
v.	O Pro73	$N^{\eta 1}$ Arg78
vi.	O (Ala/Val)80	$N^{\eta 2}$ Arg78
vii.	N His79	$O^{\delta 2}$ Asp82
4. Water mediated interactions		
i.	N Gly84	Water 14 (PA numbering)
ii.	O Gly71	Water 14, Ws1
iii.	$O^{\delta 1}$ Asp123	Water 14, Ws1
Iv	N Ala/Leu/Thr/Asp/Glu/Phe66	Water 13, Ws5
v.	N Ala/Val80	Water 13, Ws5
Vi	N Asn64	Water/I3, Ws2
vii.	$O^{\delta 1}$ Asn64	Water 13, Ws5
viii.	O Arg78	Water 87, Ws6
ix.	Water 13, Ws5	Water 87, Ws6