Supporting Information for:

Determinants of the Lead(II) Affinity in *pbrR* Protein: A Computational Study

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Table S1. Charges on atoms in the QM region in various models: assigned by MM and calculated by QM (we used those in the subsequent QM/MM calculation). Charges are in atomic units (a.u.).

Charges assigned to:	Charges assigned by:	Models			
		A	B, C, D	E, F, G	H
Pb	MM	2.000	2.000	2.000	2.000
	QM	1.110	0.845	0.694	0.614
S (thiol)	MM	-0.275	-0.335	-0.335	-
	QM	-0.200	-0.258	-0.285	-
S (thiolate)	MM	-	-0.900	-0.900	-0.900
	QM	-	-0.432	-0.620	-0.698
H (thiol sulfhydryl)	MM	0.095	0.155	0.155	-
	QM	0.240	0.239	0.214	-
CH3 (thiol)	MM	1.180	0.180	0.180	-
	QM	0.257	0.227	0.124	-
CH3 (thiolate)	MM	-	-0.100	-0.100	-0.100
	QM	-	0.172	0.246	0.160

Table S2. Predicted *pKa* values of the residues composing the (Cys)3 motif of apo *pbrR* in either monomer or homodimer calculated by using the H++ web server.

Residue	monomer	homodimer	
		chain I	chain II
Cys78	8.5	>12.0	>12.0
Cys113	9.3	>12.0	>12.0
Cys122	8.7	>12.0	9.6

Table S3. Protonation state, total charge, and assigned labels of the eight investigated QM regions of the Pb(II)-*pbrR* system.

Protonation State	Charge	Model
Cys78' (neutral), Cys113 (neutral), Cys122 (neutral)	+2	A
Cys78' (deprotonated), Cys113 (neutral), Cys122 (neutral)	+1	B
Cys78' (neutral), Cys113 (deprotonated), Cys122 (neutral)	+1	C
Cys78' (neutral), Cys113 (neutral), Cys122 (deprotonated)	+1	D
Cys78' (deprotonated), Cys113 (deprotonated), Cys122 (neutral)	0	E
Cys78' (deprotonated), Cys113 (neutral), Cys122 (deprotonated)	0	F
Cys78' (neutral), Cys113 (deprotonated), Cys122 (deprotonated)	0	G
Cys78' (deprotonated), Cys113 (deprotonated), Cys122 (deprotonated)	-1	H

Table S4. Atomic contributions and orbital combinations (percentages) for the Pb-thiol and Pb-thiolate bonds of non-protein models. Thiol and thiolate groups are denoted with HS and S, respectively.

Model	Bond	Type	Contribution	orbital combination
$[Pb(H)_3(SCH_3)_3]^{2+}$	Pb-SH ×3	2c-2e	Pb 12% , S 88%	Pb 6*p* 99% S 3*s* 11% , 3*p* 89%
$[Pb(H)_2(SCH_3)_3]^{+}$	Pb-SH ×2	2c-2e	Pb 10% , S 90%	Pb 6*p* 97% S 3*s* 12% , 3*p* 87%
	Pb-S ×1	2c-2e	Pb 20% , S 80%	Pb 6*p* 99% S 3*s* 11% , 3*p* 88%
$Pb(H)(SCH_3)_3$	Pb-S ×2	2c-2e	Pb 20% , S 80%	Pb 6*p* 99% S 3*s* 14% , 3*p* 86%
	Pb-S ×1	2c-2e	Pb 7% , S 93%	Pb 6*p* 99% S 3*p* 99%
	HS-Pb-S ×1	3c-4e	HS-Pb 46% , Pb-S 54%	-
	S-Pb-S ×1	3c-4e	HS-Pb 46% , Pb-S 54%	-
$[Pb(SCH_3)_3]^{-}$	Pb-S ×3	2c-2e	Pb 16% , S 84%	Pb 6*p* 97% S 3*s* 14% , 3*p* 86%

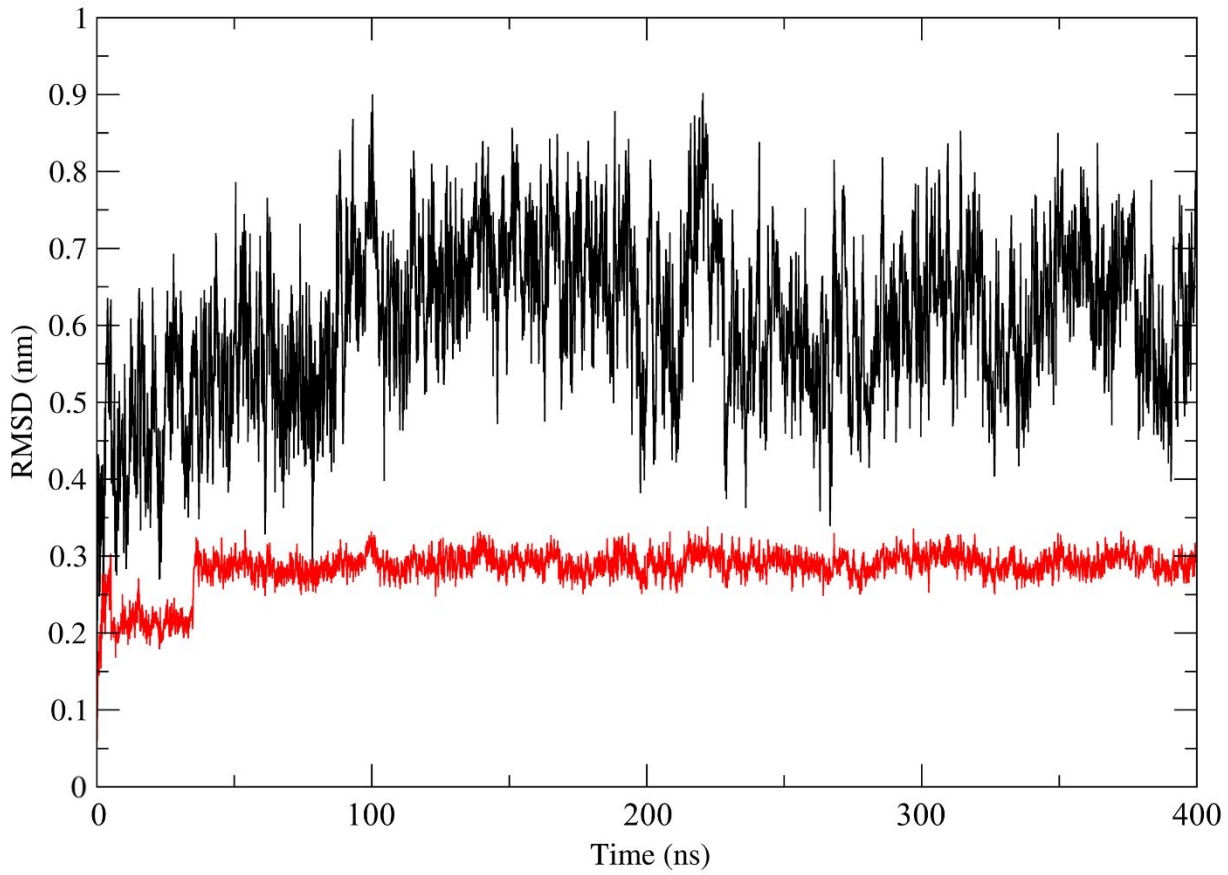

Figure S1. RMSD calculated for all backbone atoms (black|dark) and for the metal-binding motif Cys_3 (red|light) atoms.

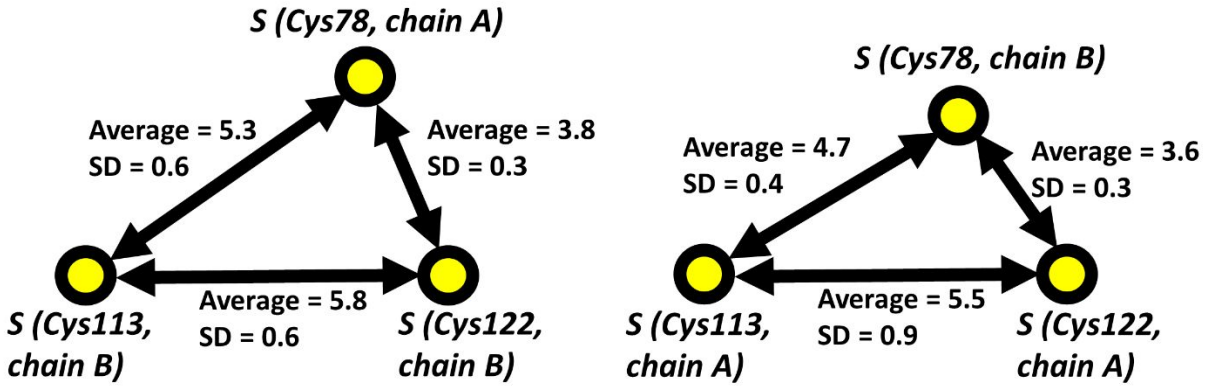

Figure S2. Average S-S minimal distances in the MD simulation of apo-*pbrR* calculated for both metal-binding loci.

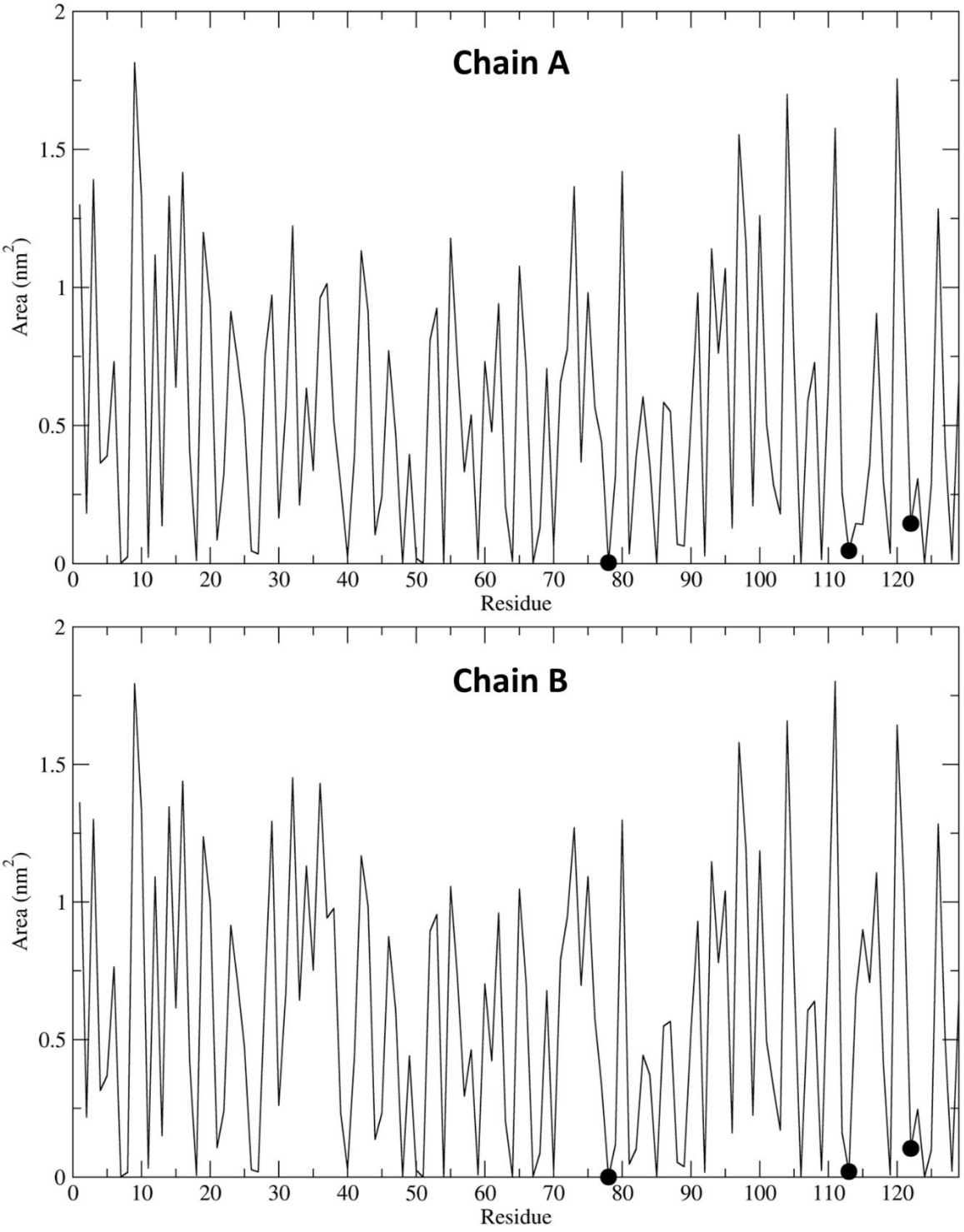

Figure S3. Solvent-accessible area per residue over the trajectory for chains A and B. Residues forming the metal-binding motif Cys78, Cys113, and Cys122 are highlighted with dots.