Supplementary Information

Mutation effects on charge transport through the p58c iron-sulfur protein

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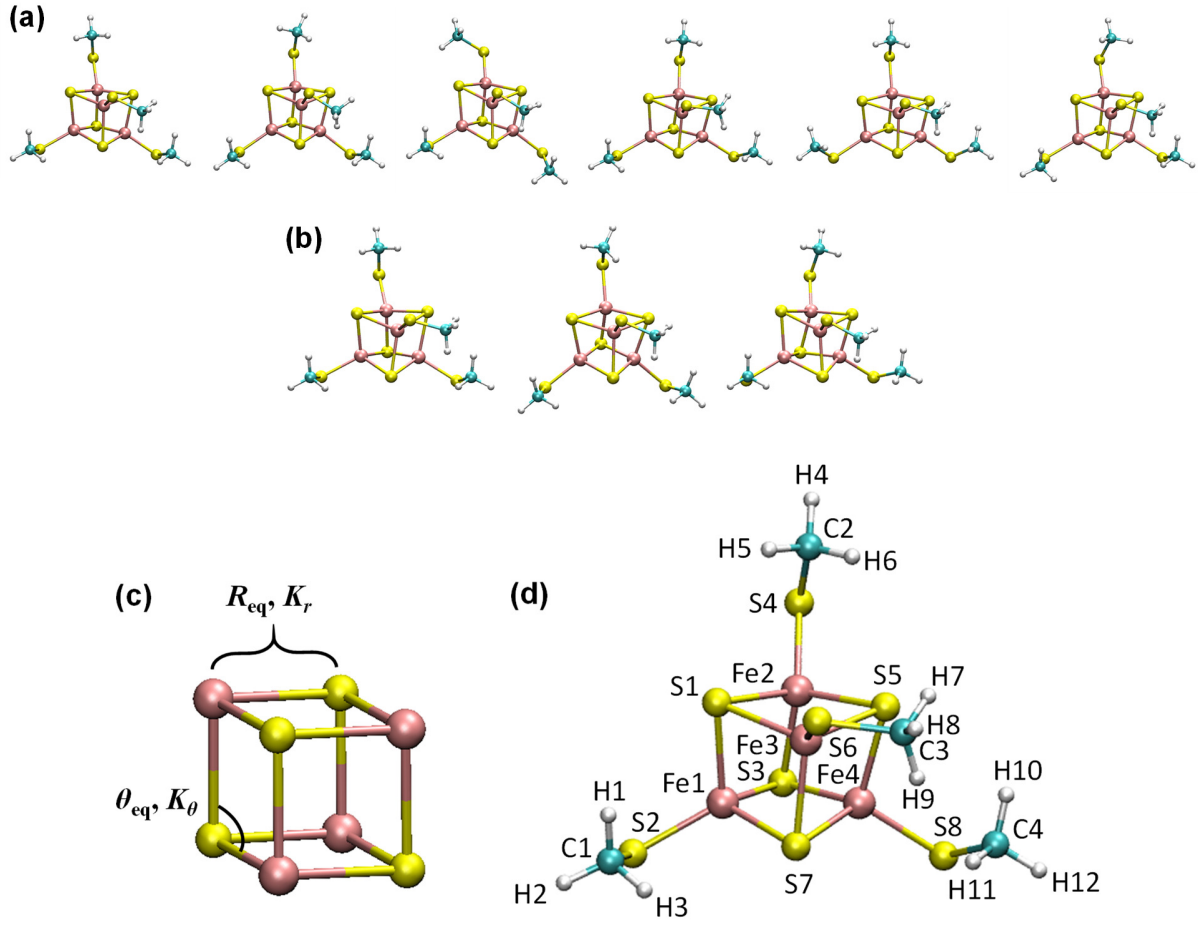

Fig. S1 Optimized geometries of the (a) oxidized and (b) reduced iron-sulfur cluster with different redox layer assignments. The corresponding force fields (FFs), which are detailed in the following tables, are named $\mathbf{1}_{3+}$ to $\mathbf{6}_{3+}$ and $\mathbf{1}_{2+}$ to $\mathbf{3}_{2+}$ for the cluster structures in (a) and (b) (from left to right), respectively. The sets $\mathbf{A}_{3+}$ and $\mathbf{A}_{2+}$ of FF parameters result from averaging over the two groups of layer assignment-specific FFs. Panel (c) illustrates the FF parameters whose values are reported in the tables. Panel (d) shows the atom notation in the FFs.

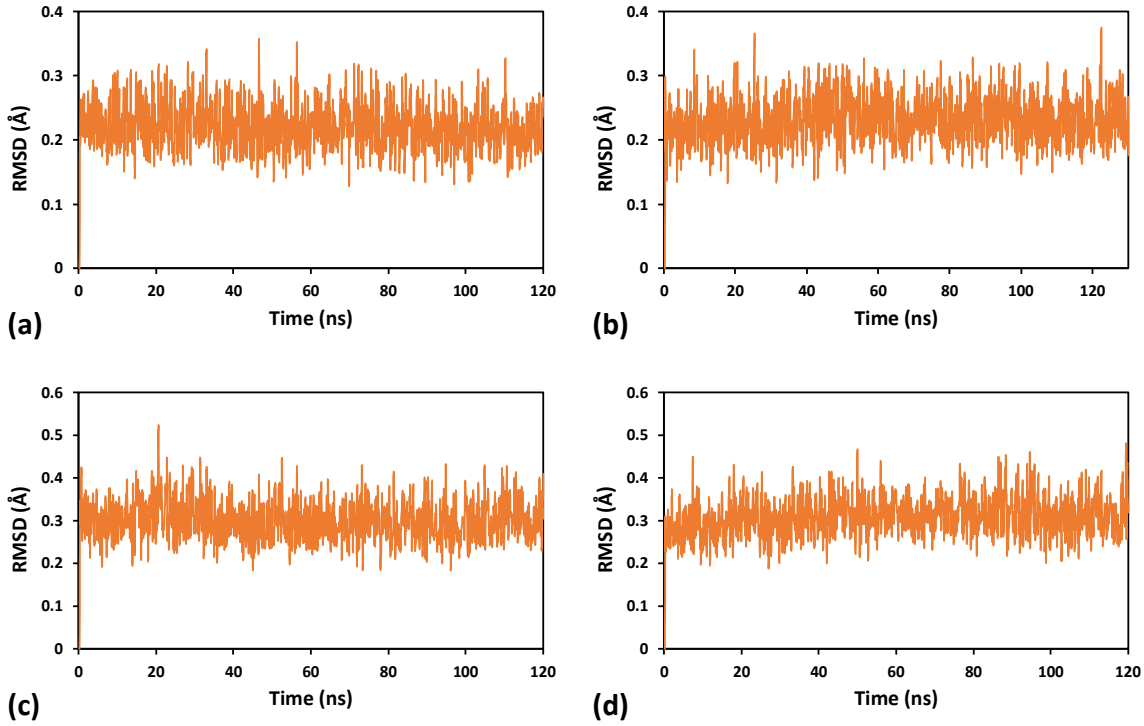

Fig. S2 RMSD (along the MD production run for the WT p58c protein with oxidized iron-sulfur cluster, in complex with the RNA/DNA duplex) for (a, b) the model system $[Fe_4S_4(SCH_3)_4]^{1-}$ used to obtain the FFs, excluding the saturation hydrogen atoms, and (c,d) the oxidized cluster together with the full Cys ligand residues. The (a, c) $\mathbf{A}_{3+}$ and $\mathbf{3}_{3+}$ (b, d) results are shown. The average RMSD value and pertinent standard deviation are: (a) 0.219 $\pm$ 0.036, (b) 0.233 $\pm$ 0.037, (c) 0.299 $\pm$ 0.046, and (d) 0.313 +/- 0.045.

Table S1. Interatomic distances R_{eq} (Å) in the six optimized geometries (denoted $\mathbf{1}_{3+}$ to $\mathbf{6}_{3+}$) of the $[Fe_4S_4(SCH_3)_4]^{1-}$ model system, which contains the oxidized iron-sulfur cluster $[Fe_4S_4]^{3+}$, and their average values.

bond	$\mathbf{1}_{3+}$	$\mathbf{2}_{3+}$	$\mathbf{3}_{3+}$	$\mathbf{4}_{3+}$	$\mathbf{5}_{3+}$	$\mathbf{6}_{3+}$	average
Fe1-S1	2.37	2.36	2.38	2.39	2.27	2.38	2.36
Fe1-S2	2.25	2.25	2.25	2.22	2.22	2.22	2.24
C4-H10	1.09	1.09	1.09	1.09	1.09	1.09	1.09
Fe1-S3	2.36	2.37	2.33	2.27	2.37	2.37	2.35
S8-C4	1.85	1.85	1.85	1.85	1.85	1.85	1.85
Fe4-S8	2.22	2.25	2.23	2.25	2.23	2.25	2.24
Fe1-S7	2.35	2.36	2.39	2.36	2.38	2.26	2.35
S1-Fe2	2.37	2.39	2.26	2.35	2.39	2.39	2.36
S1-Fe3	2.26	2.34	2.34	2.35	2.33	2.33	2.33
S2-C1	1.85	1.85	1.85	1.85	1.85	1.85	1.85
C1-H1	1.09	1.09	1.09	1.09	1.09	1.09	1.09
C1-H2	1.09	1.09	1.09	1.09	1.09	1.09	1.09
C1-H3	1.09	1.09	1.09	1.09	1.09	1.09	1.09
Fe2-S3	2.36	2.27	2.39	2.36	2.34	2.37	2.35
Fe2-S4	2.25	2.22	2.22	2.25	2.25	2.22	2.24
C4-H12	1.09	1.09	1.09	1.09	1.09	1.09	1.09
Fe2-S5	2.35	2.37	2.37	2.36	2.39	2.26	2.35
C4-H11	1.09	1.09	1.09	1.09	1.09	1.09	1.09
S3-Fe4	2.27	2.35	2.36	2.36	2.37	2.35	2.34
S4-C2	1.85	1.85	1.85	1.85	1.85	1.85	1.85
C2-H4	1.09	1.09	1.09	1.09	1.09	1.09	1.09
C2-H5	1.09	1.09	1.09	1.09	1.09	1.09	1.09
C2-H6	1.09	1.09	1.09	1.09	1.09	1.09	1.09
Fe3-S5	2.37	2.38	2.34	2.27	2.34	2.35	2.34
Fe3-S6	2.23	2.23	2.25	2.23	2.25	2.25	2.24
Fe3-S7	2.37	2.28	2.34	2.38	2.34	2.35	2.34
S5-Fe4	2.37	2.34	2.38	2.36	2.26	2.37	2.35
S6-C3	1.85	1.85	1.85	1.85	1.85	1.85	1.85
C3-H7	1.09	1.09	1.09	1.09	1.09	1.09	1.09
C3-H8	1.09	1.09	1.09	1.09	1.09	1.09	1.09
C3-H9	1.09	1.09	1.09	1.09	1.09	1.09	1.09
Fe4-S7	2.37	2.36	2.26	2.35	2.38	2.37	2.35

Table S2. Bond (stretching) force constants K_r (kcal mol^{-1} Å^{-2}) in the six optimized geometries of the model system with oxidized cluster and their average values.

bond	$\mathbf{1}_{3+}$	$\mathbf{2}_{3+}$	$\mathbf{3}_{3+}$	$\mathbf{4}_{3+}$	$\mathbf{5}_{3+}$	$\mathbf{6}_{3+}$	average
Fe1-S1	50.09	50.74	45.74	47.40	78.59	47.29	53.31
Fe1-S2	111.87	111.30	106.73	120.00	118.57	118.99	114.58
C4-H10	366.94	364.47	368.31	366.37	369.34	364.92	366.72
Fe1-S3	48.63	46.86	57.78	78.55	51.88	52.70	56.07
S8-C4	135.73	138.23	137.45	138.51	137.89	139.13	137.82
Fe4-S8	119.73	110.16	116.93	109.90	117.79	107.78	113.72
Fe1-S7	53.35	51.42	42.68	52.69	47.55	79.21	54.48
S1-Fe2	50.30	47.35	79.76	51.94	42.33	45.81	52.91
S1-Fe3	82.72	58.89	57.87	57.50	59.76	59.73	62.75
S2-C1	138.85	138.53	139.50	136.02	136.64	136.25	137.63
C1-H1	365.03	365.15	364.30	367.48	369.69	366.88	366.42
C1-H2	365.36	365.22	364.85	367.34	367.05	367.21	366.17
C1-H3	365.52	365.78	365.08	368.21	368.22	368.95	366.96
Fe2-S3	49.42	78.66	47.47	48.56	55.11	52.64	55.31
Fe2-S4	110.59	121.03	116.88	111.23	105.77	118.33	113.97
C4-H12	367.41	365.31	366.92	365.29	367.18	364.88	366.16
Fe2-S5	52.77	52.11	51.26	53.19	42.18	80.24	55.29
C4-H11	366.97	365.13	370.07	363.99	367.48	364.04	366.28
S3-Fe4	78.89	51.87	53.07	50.52	52.10	54.33	56.80
S4-C2	138.72	135.94	137.39	138.64	138.87	136.37	137.66
C2-H4	364.72	367.43	366.67	365.59	364.97	367.31	366.11
C2-H5	365.47	368.60	370.18	365.33	365.21	367.07	366.98
C2-H6	366.13	366.20	369.96	365.25	363.94	368.94	366.74
Fe3-S5	52.78	48.84	53.21	78.34	58.91	53.27	57.56
Fe3-S6	118.69	117.97	109.28	116.60	108.61	107.24	113.06
Fe3-S7	50.53	74.13	58.53	47.70	53.93	55.38	56.70
S5-Fe4	50.57	53.77	47.50	51.58	80.61	48.37	55.40
S6-C3	135.88	135.76	138.76	136.49	138.17	138.86	137.32
C3-H7	367.22	368.62	365.05	369.11	366.52	365.59	367.02
C3-H8	366.64	367.70	365.71	366.93	365.81	364.97	366.29
C3-H9	367.96	365.37	365.44	366.93	364.71	366.00	366.07
Fe4-S7	51.63	53.89	80.80	52.34	48.84	46.50	55.67

Table S3. Angles θ_{eq} (°) for the six optimized geometries of the model system with oxidized cluster and their average values.

angle	$\mathbf{1}_{3+}$	$\mathbf{2}_{3+}$	$\mathbf{3}_{3+}$	$\mathbf{4}_{3+}$	$\mathbf{5}_{3+}$	$\mathbf{6}_{3+}$	average
C4-S8-Fe4	98.27	97.38	101.78	98.70	101.19	98.79	99.35
Fe1-S1-Fe2	71.01	76.46	78.30	76.34	78.07	81.65	76.97
Fe1-S1-Fe3	78.48	77.11	70.44	82.03	78.74	76.59	77.23
Fe1-S2-C1	97.78	98.26	99.65	99.15	101.43	99.50	99.30
Fe1-S3-Fe2	71.22	78.50	76.89	78.41	77.00	82.37	77.40
Fe1-S3-Fe4	78.15	71.65	77.10	78.16	82.45	76.57	77.35
Fe1-S7-Fe3	76.73	78.31	70.34	81.81	76.33	78.48	77.00
Fe1-S7-Fe4	76.49	71.73	78.11	76.49	82.05	78.08	77.16
Fe2-S1-Fe3	78.28	81.88	78.55	76.85	70.38	76.52	77.08
Fe2-S3-Fe4	78.37	78.48	82.52	71.73	77.08	76.73	77.48
Fe2-S4-C2	98.47	99.41	102.74	97.92	99.06	99.71	99.55
Fe2-S5-Fe3	76.55	81.55	76.32	78.31	70.25	78.44	76.90
Fe2-S5-Fe4	76.58	76.70	82.48	71.75	78.20	78.35	77.34
Fe3-S5-Fe4	81.72	76.97	76.30	78.82	78.81	69.11	76.96
Fe3-S6-C3	97.99	99.86	98.09	100.15	98.58	99.07	98.96
Fe3-S7-Fe4	81.67	78.73	78.79	76.80	76.52	69.10	76.94
H1-C1-H2	109.39	109.32	109.33	109.60	109.85	109.41	109.48
H1-C1-H3	109.18	109.18	109.14	109.55	109.49	109.58	109.35
H11-C4-H10	109.41	109.13	109.50	109.15	109.45	108.91	109.26
H11-C4-H12	109.62	109.44	109.83	109.16	109.40	109.45	109.48
H11-C4-S8	110.05	110.30	110.04	110.60	110.25	110.16	110.23
H12-C4-H10	109.58	109.26	109.49	109.54	109.81	109.40	109.51
H2-C1-H3	109.30	109.41	109.42	109.64	109.51	109.76	109.51
H4-C2-H5	109.23	109.80	109.63	109.31	109.46	109.36	109.47
H4-C2-H6	109.19	109.28	109.65	109.39	109.33	109.83	109.44
H5-C2-H6	109.47	109.50	109.55	109.22	109.00	109.51	109.38
H7-C3-H8	109.56	109.85	109.33	109.82	109.60	109.58	109.62
H7-C3-H9	109.73	109.40	109.20	109.42	109.21	109.00	109.33
H8-C3-H9	109.34	109.15	109.49	109.34	109.28	109.42	109.34
S1-Fe1-S2	114.83	119.39	113.36	116.36	116.93	116.69	116.26
S1-Fe1-S3	108.17	100.03	100.01	102.06	102.52	97.04	101.64
S1-Fe1-S7	99.53	99.36	107.38	96.51	101.01	100.88	100.78
S1-Fe2-S3	108.34	102.23	102.03	100.27	99.68	96.96	101.59

S1-Fe2-S4	114.45	116.44	118.01	117.93	111.41	116.44	115.78
S1-Fe2-S5	99.75	96.61	101.54	99.64	107.26	101.07	100.98
S1-Fe3-S5	102.33	97.41	100.14	102.34	110.92	100.16	102.22
S1-Fe3-S6	121.14	120.53	113.87	119.95	114.29	120.52	118.38
S1-Fe3-S7	101.99	102.29	110.53	96.88	100.24	100.02	101.99
S2-C1-H1	110.39	110.45	110.29	110.16	109.92	110.16	110.23
S2-C1-H2	108.27	108.25	108.50	107.92	107.77	107.84	108.09
S2-C1-H3	110.30	110.22	110.15	109.95	110.27	110.07	110.16
S2-Fe1-S3	113.52	113.50	123.73	119.40	118.55	119.62	118.05
S2-Fe1-S7	118.84	115.23	110.92	116.61	117.84	116.79	116.04
S3-Fe1-S7	100.09	107.28	99.61	102.40	96.53	102.38	101.38
S3-Fe2-S4	113.89	120.14	117.02	114.17	125.11	120.21	118.42
S3-Fe2-S5	99.90	101.82	96.21	107.53	99.45	102.05	101.16
S3-Fe4-S5	101.93	99.92	96.38	107.56	102.49	99.47	101.29
S3-Fe4-S7	102.27	108.03	102.39	100.09	96.67	99.72	101.53
S4-C2-H4	110.51	108.03	107.72	108.20	108.51	107.85	108.47
S4-C2-H5	108.19	109.63	110.18	110.36	110.23	110.26	109.81
S4-C2-H6	110.23	110.58	110.08	110.33	110.29	110.01	110.26
S4-Fe2-S5	118.67	115.97	118.45	115.30	112.04	116.63	116.18
S5-Fe3-S6	114.99	115.41	117.44	115.88	112.75	110.27	114.46
S5-Fe3-S7	97.03	101.22	100.11	101.51	99.84	111.07	101.79
S5-Fe4-S7	97.00	99.89	101.23	99.82	101.06	109.67	101.45
S6-C3-H7	108.05	109.26	110.34	110.09	110.17	110.13	109.67
S6-C3-H8	110.19	108.33	108.22	107.89	108.19	108.36	108.53
S6-C3-H9	109.95	110.84	110.24	110.26	110.37	110.34	110.33
S6-Fe3-S7	115.77	116.62	113.29	116.99	117.35	113.71	115.62
S8-C4-H10	110.16	110.39	110.19	110.16	110.09	110.38	110.23
S8-C4-H12	108.01	108.30	107.77	108.21	107.82	108.53	108.11
S8-Fe4-S3	121.08	115.95	118.11	114.87	118.63	124.52	118.86
S8-Fe4-S5	115.14	116.56	118.25	113.07	116.26	111.39	115.11
S8-Fe4-S7	115.81	114.42	117.01	119.56	118.36	110.77	115.99

Table S4. Angle (bending) force constants K_θ (kcal mol^{-1} rad^{-2}) in the six optimized geometries of the model system with oxidized cluster and their average values.

angle	$\mathbf{1}_{3+}$	$\mathbf{2}_{3+}$	$\mathbf{3}_{3+}$	$\mathbf{4}_{3+}$	$\mathbf{5}_{3+}$	$\mathbf{6}_{3+}$	average
C4-S8-Fe4	47.14	23.51	52.15	21.78	50.04	56.07	41.78
Fe1-S1-Fe2	28.57	48.09	33.14	52.97	35.31	37.59	39.28
Fe1-S1-Fe3	33.16	46.02	23.00	35.74	35.57	49.16	37.11
Fe1-S2-C1	26.86	25.37	54.27	48.26	52.38	34.21	40.23
Fe1-S3-Fe2	19.88	32.86	49.42	32.49	48.78	32.53	35.99
Fe1-S3-Fe4	33.35	20.41	49.43	34.98	34.69	46.43	36.55
Fe1-S7-Fe3	49.95	33.20	21.51	35.49	49.74	34.70	37.43
Fe1-S7-Fe4	54.88	31.11	34.93	53.32	41.67	35.37	41.88
Fe2-S1-Fe3	31.96	37.15	35.00	47.15	23.73	46.65	36.94
Fe2-S3-Fe4	32.44	31.69	31.92	22.58	46.46	43.17	34.71
Fe2-S4-C2	25.29	47.30	57.59	26.55	52.69	39.29	41.45
Fe2-S5-Fe3	49.90	34.67	53.28	34.28	23.50	35.41	38.51
Fe2-S5-Fe4	54.60	52.09	38.44	31.51	33.42	36.12	41.03
Fe3-S5-Fe4	34.46	46.82	47.55	30.17	33.66	23.71	36.06
Fe3-S6-C3	47.73	39.16	35.12	46.61	36.45	52.55	42.94
Fe3-S7-Fe4	34.54	31.34	32.78	49.22	49.13	25.15	37.03
H1-C1-H2	42.92	43.27	43.05	42.73	42.52	42.86	42.89
H1-C1-H3	42.19	42.42	42.51	42.11	41.28	41.72	42.04
H11-C4-H10	41.74	42.43	41.15	42.10	41.12	42.24	41.80
H11-C4-H12	42.30	42.39	43.08	42.98	42.96	42.40	42.68
H11-C4-S8	42.90	43.96	42.42	42.38	41.97	42.28	42.65
H12-C4-H10	42.65	42.83	43.19	42.39	42.32	43.42	42.80
H2-C1-H3	42.34	42.17	41.81	41.88	43.30	41.97	42.25
H4-C2-H5	43.11	41.78	43.28	42.68	42.38	43.33	42.76
H4-C2-H6	42.16	42.55	43.32	42.72	43.20	42.27	42.70
H5-C2-H6	42.44	42.01	40.94	42.07	42.29	41.22	41.83
H7-C3-H8	42.73	41.52	42.69	42.46	42.27	42.28	42.32
H7-C3-H9	42.24	42.45	42.25	41.71	41.76	42.46	42.15
H8-C3-H9	41.96	42.53	42.45	43.21	42.99	43.32	42.74
S1-Fe1-S2	27.00	24.57	29.01	27.25	23.59	23.58	25.83
S1-Fe1-S3	27.28	36.02	35.09	50.26	49.93	59.49	43.01
S1-Fe1-S7	43.18	41.10	37.73	62.71	54.60	52.02	48.56
S1-Fe2-S3	25.30	49.48	50.96	34.64	34.28	55.42	41.68

S1-Fe2-S4	22.83	27.46	29.91	22.54	33.09	25.04	26.81
S1-Fe2-S5	43.51	56.90	50.13	42.40	37.30	51.61	46.97
S1-Fe3-S5	48.38	63.16	38.12	50.65	22.79	36.96	43.34
S1-Fe3-S6	28.31	30.33	19.81	41.65	19.03	29.87	28.17
S1-Fe3-S7	47.83	49.52	18.81	62.18	39.43	39.69	42.91
S2-C1-H1	43.60	43.64	41.85	43.28	42.29	41.99	42.78
S2-C1-H2	41.89	40.94	41.39	42.43	42.81	41.52	41.83
S2-C1-H3	43.67	43.86	42.10	41.96	41.63	42.75	42.66
S2-Fe1-S3	19.20	17.05	33.39	28.71	45.57	39.75	30.61
S2-Fe1-S7	23.01	28.98	29.20	26.98	31.96	24.84	27.49
S3-Fe1-S7	36.49	35.49	32.78	46.86	61.34	48.62	43.59
S3-Fe2-S4	16.34	28.11	33.74	17.70	32.07	34.86	27.14
S3-Fe2-S5	36.34	47.36	60.71	30.82	34.55	50.65	43.41
S3-Fe4-S5	48.59	36.55	59.96	30.23	51.77	34.66	43.62
S3-Fe4-S7	48.98	25.06	47.66	39.70	62.09	34.75	43.04
S4-C2-H4	42.89	44.47	40.58	41.44	42.94	41.81	42.35
S4-C2-H5	41.23	37.10	41.86	43.66	42.45	42.53	41.47
S4-C2-H6	43.61	41.90	42.08	43.03	39.75	42.67	42.17
S4-Fe2-S5	20.49	26.60	36.20	26.88	38.91	21.40	28.41
S5-Fe3-S6	26.23	25.66	28.11	24.29	26.10	30.67	26.84
S5-Fe3-S7	62.12	52.22	43.38	51.66	45.11	23.97	46.41
S5-Fe4-S7	62.15	41.23	52.12	39.69	51.89	38.61	47.61
S6-C3-H7	41.97	39.43	43.41	42.84	43.49	41.71	42.14
S6-C3-H8	41.68	44.88	40.76	41.02	41.92	42.27	42.09
S6-C3-H9	42.46	41.24	43.58	42.36	43.21	42.26	42.52
S6-Fe3-S7	26.22	26.03	26.78	28.94	29.08	31.57	28.10
S8-C4-H10	42.89	43.63	41.38	43.30	41.91	43.95	42.84
S8-C4-H12	39.65	39.93	40.89	41.86	41.53	39.01	40.48
S8-Fe4-S3	28.31	14.74	41.92	13.65	43.53	27.75	28.32
S8-Fe4-S5	27.59	25.12	23.55	23.19	25.47	37.73	27.11
S8-Fe4-S7	27.17	26.52	27.04	22.37	29.86	34.42	27.90

Table S5. Restraint electrostatic potential (RESP) partial charges on the atoms of the six optimized geometries of the model system with oxidized cluster and their average values. The charges were computed using DFT at the B3LYP/6-31g* level of computational accuracy.

atom	$\mathbf{1}_{3+}$	$\mathbf{2}_{3+}$	$\mathbf{3}_{3+}$	$\mathbf{4}_{3+}$	$\mathbf{5}_{3+}$	$\mathbf{6}_{3+}$	average
Fe1	0.59973	0.60853	0.58623	0.69798	0.74986	0.72213	0.66074
S1	-0.50546	-0.57699	-0.50808	-0.56556	-0.52598	-0.59592	-0.54633
S2	-0.59748	-0.59812	-0.62187	-0.56538	-0.56489	-0.56544	-0.58553
C1	0.42369	0.42248	0.42837	0.47130	0.43459	0.46036	0.44013
H1	-0.08496	-0.08981	-0.08253	-0.08457	-0.08555	-0.08809	-0.08592
H2	-0.05757	-0.05596	-0.05918	-0.07038	-0.05251	-0.06356	-0.05986
H3	-0.09870	-0.09870	-0.09870	-0.09870	-0.09870	-0.09870	-0.09870
Fe2	0.60125	0.69276	0.78408	0.57785	0.55494	0.71655	0.65457
S3	-0.43869	-0.46046	-0.56996	-0.44980	-0.53603	-0.51519	-0.49502
S4	-0.60082	-0.55541	-0.56201	-0.58786	-0.61228	-0.56127	-0.57994
C2	0.44670	0.44244	0.41510	0.41306	0.41985	0.45148	0.43144
H4	-0.10043	-0.06071	-0.04435	-0.05359	-0.06010	-0.05820	-0.06290
H5	-0.06220	-0.07406	-0.08595	-0.08454	-0.07536	-0.09142	-0.07892
H6	-0.09870	-0.09870	-0.09870	-0.09870	-0.09870	-0.09870	-0.09870
Fe3	0.76680	0.82225	0.68440	0.80772	0.77200	0.77975	0.77215
S5	-0.55222	-0.58859	-0.62845	-0.51013	-0.53892	-0.56184	-0.56336
S6	-0.59119	-0.59062	-0.61103	-0.59716	-0.62894	-0.63102	-0.60833
C3	0.45606	0.39001	0.42910	0.42892	0.43153	0.36828	0.41732
H7	-0.06197	-0.05377	-0.07837	-0.08659	-0.08530	-0.05219	-0.06970
H8	-0.09197	-0.04787	-0.05937	-0.04826	-0.05562	-0.04241	-0.05758
H9	-0.09870	-0.09870	-0.09870	-0.09870	-0.09870	-0.09870	-0.09870
Fe4	0.62687	0.60591	0.75755	0.59044	0.74701	0.58700	0.65246
S7	-0.56041	-0.54469	-0.51325	-0.59103	-0.63213	-0.57391	-0.56924
S8	-0.54326	-0.60281	-0.57254	-0.60206	-0.57369	-0.61104	-0.58423
C4	0.46060	0.46662	0.51789	0.47550	0.51114	0.42587	0.47627
H10	-0.07060	-0.08328	-0.09862	-0.09251	-0.10503	-0.06536	-0.08590
H11	-0.06769	-0.07305	-0.11236	-0.07853	-0.09379	-0.03974	-0.07753
H12	-0.09870	-0.09870	-0.09870	-0.09870	-0.09870	-0.09870	-0.09870

Table S6. Interatomic distances R_{eq} (Å) for the three optimized geometries (denoted $\mathbf{1}_{2+}$ to $\mathbf{3}_{2+}$) of the $[Fe_4S_4(SCH_3)_4]^{2-}$ model system, which corresponds to the reduced iron-sulfur cluster $[Fe_4S_4]^{2+}$, and their average values.

bond	$\mathbf{1}_{2+}$	$\mathbf{2}_{2+}$	$\mathbf{3}_{2+}$	average
Fe1-S1	2.37	2.34	2.38	2.36
Fe1-S2	2.28	2.28	2.28	2.28
C4-H11	1.09	1.09	1.09	1.09
Fe1-S3	2.36	2.36	2.34	2.35
Fe4-S8	2.28	2.28	2.28	2.28
S8-C4	1.85	1.85	1.85	1.85
Fe1-S7	2.34	2.36	2.39	2.36
S1-Fe2	2.37	2.39	2.34	2.37
S1-Fe3	2.33	2.33	2.34	2.33
S2-C1	1.85	1.85	1.85	1.85
C1-H1	1.09	1.09	1.09	1.09
C1-H2	1.09	1.09	1.09	1.09
C1-H3	1.09	1.09	1.09	1.09
Fe2-S3	2.36	2.34	2.36	2.35
Fe2-S4	2.28	2.28	2.28	2.28
C4-H12	1.09	1.09	1.09	1.09
Fe2-S5	2.33	2.39	2.36	2.36
C4-H10	1.09	1.09	1.09	1.09
S3-Fe4	2.34	2.36	2.36	2.35
S4-C2	1.85	1.85	1.85	1.85
C2-H4	1.09	1.09	1.09	1.09
C2-H5	1.09	1.09	1.09	1.09
C2-H6	1.09	1.09	1.09	1.09
Fe3-S5	2.36	2.34	2.34	2.35
Fe3-S6	2.28	2.28	2.28	2.28
Fe4-S7	2.37	2.36	2.34	2.35
Fe3-S7	2.35	2.34	2.34	2.34
S5-Fe4	2.36	2.34	2.36	2.35
S6-C3	1.85	1.85	1.85	1.85
C3-H7	1.09	1.09	1.09	1.09
C3-H8	1.09	1.09	1.09	1.09
C3-H9	1.09	1.09	1.09	1.09

Table S7. Bond (stretching) force constants K_r (kcal mol^{-1} Å^{-2}) for the three optimized geometries of the model system with reduced cluster and their average values.

bond	$\mathbf{1}_{2+}$	$\mathbf{2}_{2+}$	$\mathbf{3}_{2+}$	average
Fe1-S1	52.29	54.79	47.84	51.64
Fe1-S2	99.73	97.86	94.34	97.31
C4-H11	361.50	363.03	362.34	362.29
Fe1-S3	51.81	50.81	56.88	53.17
Fe4-S8	95.03	97.51	97.77	96.77
S8-C4	141.36	140.98	141.03	141.12
Fe1-S7	57.70	52.43	44.84	51.66
S1-Fe2	50.93	44.95	54.58	50.15
S1-Fe3	59.61	60.36	59.25	59.74
S2-C1	140.97	141.04	140.21	140.74
C1-H1	363.05	362.95	362.01	362.67
C1-H2	361.89	361.98	361.96	361.94
C1-H3	363.52	364.06	362.68	363.42
Fe2-S3	51.07	56.30	51.48	52.95
Fe2-S4	97.66	92.70	98.24	96.20
C4-H12	361.69	361.76	361.79	361.75
Fe2-S5	56.76	43.87	52.44	51.03
C4-H10	363.51	362.78	364.54	363.61
S3-Fe4	55.65	51.87	51.93	53.15
S4-C2	141.08	140.10	141.19	140.79
C2-H4	362.30	361.94	362.35	362.20
C2-H5	363.94	363.98	363.23	363.71
C2-H6	362.80	360.80	363.26	362.29
Fe3-S5	52.33	59.73	55.90	55.99
Fe3-S6	93.69	97.01	96.36	95.68
Fe4-S7	51.03	54.04	56.75	53.94
Fe3-S7	55.88	56.08	59.84	57.27
S5-Fe4	52.37	57.42	53.62	54.47
S6-C3	141.06	140.62	141.12	140.93
C3-H7	363.99	363.73	362.97	363.56
C3-H8	361.59	362.35	362.38	362.11
C3-H9	363.62	362.93	363.55	363.37

Table S8. Angles θ_{eq}(°) in the three optimized geometries of the model system with reduced cluster and their average values.

angle	$\mathbf{1}_{2+}$	$\mathbf{2}_{2+}$	$\mathbf{3}_{2+}$	average
S1-Fe1-S2	114.02	117.96	112.13	114.70
S1-Fe1-S3	109.67	101.03	100.20	103.63
S1-Fe1-S7	99.86	99.60	108.98	102.81
S2-Fe1-S3	114.23	113.69	122.71	116.88
S2-Fe1-S7	116.80	113.56	111.43	113.93
S3-Fe1-S7	100.63	109.50	100.01	103.38
Fe1-S1-Fe3	76.07	76.24	69.30	73.87
Fe1-S1-Fe2	70.08	75.80	75.75	73.87
Fe2-S1-Fe3	76.09	69.64	76.18	73.97
Fe1-S2-C1	96.96	97.92	97.68	97.52
S2-C1-H1	110.30	110.44	110.34	110.36
S2-C1-H2	108.84	108.80	108.98	108.87
S2-C1-H3	110.28	110.17	110.20	110.22
H1-C1-H2	109.28	109.17	109.17	109.21
H1-C1-H3	108.87	108.84	108.78	108.83
H2-C1-H3	109.24	109.41	109.34	109.33
S1-Fe2-S3	109.56	100.28	100.77	103.54
S1-Fe2-S4	114.84	111.79	118.55	115.06
S1-Fe2-S5	99.89	108.41	99.51	102.60
S3-Fe2-S4	113.53	122.10	112.96	116.20
S3-Fe2-S5	100.70	100.03	110.36	103.69
S4-Fe2-S5	116.68	112.72	113.33	114.24
Fe1-S3-Fe4	75.98	70.18	76.35	74.17
Fe2-S3-Fe4	75.84	76.36	69.51	73.90
Fe1-S3-Fe2	70.38	76.35	76.29	74.34
Fe2-S4-C2	98.28	99.31	98.13	98.57
S4-C2-H4	108.70	109.05	108.76	108.84
S4-C2-H5	110.34	110.15	110.44	110.31
S4-C2-H6	110.46	110.70	110.21	110.46
H4-C2-H5	109.34	109.42	109.17	109.31
H4-C2-H6	109.12	108.81	109.32	109.08
H5-C2-H6	108.85	108.68	108.93	108.82
S1-Fe3-S7	100.39	100.77	112.31	104.49

S1-Fe3-S5	100.32	112.11	100.51	104.31
S1-Fe3-S6	118.49	113.40	113.04	114.97
S5-Fe3-S6	110.36	113.19	116.10	113.22
S5-Fe3-S7	110.97	100.06	100.03	103.69
S6-Fe3-S7	115.08	116.01	113.55	114.88
Fe2-S5-Fe4	75.89	75.85	69.43	73.72
Fe3-S5-Fe4	69.13	76.36	75.96	73.82
Fe2-S5-Fe3	76.18	69.48	75.76	73.81
Fe3-S6-C3	99.40	97.84	97.99	98.41
S6-C3-H7	110.17	110.28	110.32	110.26
S6-C3-H8	108.86	108.80	108.76	108.80
S6-C3-H9	110.42	110.24	110.28	110.32
H7-C3-H8	109.51	109.39	109.22	109.37
H7-C3-H9	108.61	108.90	108.89	108.80
H8-C3-H9	109.25	109.21	109.36	109.27
S8-Fe4-S3	120.49	114.27	112.97	115.91
S8-Fe4-S7	112.05	113.67	118.73	114.82
S3-Fe4-S7	100.24	109.87	100.84	103.65
S3-Fe4-S5	100.46	101.17	110.45	104.02
S8-Fe4-S5	112.04	116.74	113.08	113.96
S7-Fe4-S5	110.43	99.57	99.43	103.14
Fe1-S7-Fe4	75.92	70.10	75.82	73.94
Fe4-S7-Fe3	69.14	75.99	76.31	73.81
Fe1-S7-Fe3	76.21	75.73	69.14	73.69
Fe4-S8-C4	98.13	97.07	98.51	97.90
H12-C4-H10	109.32	109.22	109.50	109.35
H11-C4-H12	109.23	109.32	109.07	109.21
H11-C4-H10	108.59	108.81	108.82	108.74
H11-C4-S8	110.27	110.24	110.54	110.35
S8-C4-H12	109.01	108.88	108.74	108.87
S8-C4-H10	100.40	110.36	110.14	106.97

Table S9. Angle (bending) force constants K_θ (kcal mol^{-1}rad^{-2}) for the three optimized geometries of the model system with reduced cluster and their average values.

angle	$\mathbf{1}_{2+}$	$\mathbf{2}_{2+}$	$\mathbf{3}_{2+}$	average
S1-Fe1-S2	29.06	27.99	44.10	33.72
S1-Fe1-S3	28.76	30.58	31.11	30.15
S1-Fe1-S7	37.17	36.01	40.97	38.05
S2-Fe1-S3	25.30	23.23	32.97	27.16
S2-Fe1-S7	27.35	30.26	19.20	25.60
S3-Fe1-S7	30.94	32.91	28.76	30.87
Fe1-S1-Fe3	35.54	32.21	22.48	30.08
Fe1-S1-Fe2	30.12	36.57	35.34	34.01
Fe2-S1-Fe3	31.35	22.61	33.06	29.00
Fe1-S2-C1	37.39	36.32	61.26	44.99
S2-C1-H1	43.48	42.80	41.06	42.45
S2-C1-H2	41.75	41.12	39.03	40.63
S2-C1-H3	43.14	43.63	42.91	43.23
H1-C1-H2	43.03	43.40	43.02	43.15
H1-C1-H3	42.39	42.54	42.54	42.49
H2-C1-H3	42.57	42.63	42.53	42.58
S1-Fe2-S3	30.37	32.26	30.58	31.07
S1-Fe2-S4	26.38	41.05	26.97	31.47
S1-Fe2-S5	34.26	42.97	35.89	37.71
S3-Fe2-S4	23.05	34.00	21.24	26.09
S3-Fe2-S5	31.63	28.21	29.54	29.79
S4-Fe2-S5	24.20	41.68	28.93	31.60
Fe1-S3-Fe4	33.43	22.19	35.02	30.21
Fe2-S3-Fe4	34.17	33.14	20.92	29.41
Fe1-S3-Fe2	22.06	33.09	32.92	29.36
Fe2-S4-C2	38.86	60.30	38.28	45.81
S4-C2-H4	40.94	43.80	42.42	42.39
S4-C2-H5	42.72	37.77	42.03	40.84
S4-C2-H6	42.95	39.57	42.62	41.71
H4-C2-H5	42.83	41.93	42.82	42.53
H4-C2-H6	43.17	43.04	42.66	42.96
H5-C2-H6	42.33	42.11	42.74	42.39
S1-Fe3-S7	33.21	33.51	18.99	28.57

S1-Fe3-S5	30.55	16.80	33.08	26.81
S1-Fe3-S6	34.82	21.10	23.73	26.55
S5-Fe3-S6	34.26	26.59	31.33	30.72
S5-Fe3-S7	29.34	37.62	38.05	35.00
S6-Fe3-S7	31.59	32.37	26.34	30.10
Fe2-S5-Fe4	34.73	32.68	28.36	31.92
Fe3-S5-Fe4	27.95	34.43	33.77	32.05
Fe2-S5-Fe3	34.38	21.56	32.84	29.60
Fe3-S6-C3	55.74	40.37	41.95	46.02
S6-C3-H7	42.00	43.08	42.73	42.60
S6-C3-H8	42.09	40.05	41.59	41.25
S6-C3-H9	41.85	42.91	42.81	42.52
H7-C3-H8	42.43	42.67	42.68	42.60
H7-C3-H9	42.27	42.31	42.39	42.32
H8-C3-H9	43.32	42.90	42.95	43.06
S8-Fe4-S3	35.52	22.59	20.66	26.26
S8-Fe4-S7	31.19	30.15	28.10	29.81
S3-Fe4-S7	28.47	27.60	32.39	29.49
S3-Fe4-S5	32.11	30.70	27.52	30.11
S8-Fe4-S5	32.99	29.03	24.72	28.91
S7-Fe4-S5	37.30	34.61	36.42	36.11
Fe1-S7-Fe4	35.13	30.60	35.69	33.81
Fe4-S7-Fe3	32.78	31.29	34.34	32.80
Fe1-S7-Fe3	36.22	33.69	24.43	31.45
Fe4-S8-C4	57.79	37.58	34.55	43.31
H12-C4-H10	43.31	42.84	42.77	42.98
H11-C4-H12	42.62	42.79	43.35	42.92
H11-C4-H10	42.36	42.52	42.31	42.39
H11-C4-S8	42.38	42.52	42.23	42.38
S8-C4-H12	40.07	41.66	40.83	40.85
S8-C4-H10	43.21	43.15	42.80	43.06

Table S10. Restraint electrostatic potential (RESP) atomic partial charges for the three optimized geometries of the model system with reduced cluster and their average values. The B3LYP/6-31g* computational setup was used.

atom	$\mathbf{1}_{2+}$	$\mathbf{2}_{2+}$	$\mathbf{3}_{2+}$	average
Fe1	0.72175	0.68155	0.67058	0.69129
S1	-0.68520	-0.70051	-0.68618	-0.69063
S2	-0.71774	-0.70080	-0.72143	-0.71332
C1	0.45856	0.43468	0.42029	0.43784
H1	-0.09179	-0.09381	-0.07244	-0.08601
H2	-0.10185	-0.09179	-0.08954	-0.09439
H3	-0.09870	-0.09870	-0.09870	-0.09870
Fe2	0.69428	0.69795	0.68768	0.69330
S3	-0.61800	-0.61975	-0.60914	-0.61563
S4	-0.70358	-0.73167	-0.70208	-0.71244
C2	0.43005	0.44057	0.43150	0.43404
H4	-0.09040	-0.09653	-0.08947	-0.09213
H5	-0.08721	-0.08335	-0.09406	-0.08821
H6	-0.09870	-0.09870	-0.09870	-0.09870
Fe3	0.84634	0.89280	0.86123	0.86679
S5	-0.70390	-0.71684	-0.67613	-0.69896
S6	-0.74539	-0.73034	-0.74179	-0.73917
C3	0.38688	0.37549	0.44672	0.40303
H7	-0.05424	-0.06324	-0.10604	-0.07450
H8	-0.08181	-0.07101	-0.08829	-0.08037
H9	-0.09870	-0.09870	-0.09870	-0.09870
Fe4	0.69640	0.69437	0.67514	0.68864
S7	-0.72918	-0.68384	-0.68181	-0.69828
S8	-0.70569	-0.69996	-0.69709	-0.70091
C4	0.34869	0.39374	0.40187	0.38143
H10	-0.04829	-0.07045	-0.06431	-0.06102
H11	-0.02389	-0.06244	-0.08042	-0.05558
H12	-0.09870	-0.09870	-0.09870	-0.09870

Table S11. Energy comparison of the six $[Fe_4S_4(SCH_3)_4]^{1-}$ structures (optimized using the B3LYP exchange-correlation functional,[1] the 6-31g** basis set, Grimme's DFT-D3 dispersion correction,[2] and the Cosmo model[3-6]), and RMSD of the $Fe_4S_4]^{3+}$ cluster with respect to the crystal structure. E_{gp} is the energy calculated with the COSMO model of a dielectric continuum environment using the electronic density optimized in gas phase. ΔE_{gp} denotes the relative energy with respect to the minimum-energy structure. The electrostatic solvation energy (ESE) considered in the table is the difference between E_{gp} and the energy that is calculated using the electronic density optimized in the presence of the dielectric continuum. Therefore, ΔE_{gp} measures the difference in solute-solvent electrostatic interaction energy due to the solvent effect on the electronic charge distribution of the solute. The structural fluctuations of the iron-sulfur cluster and surroundings, as well as the related polarization, are expected to produce energy fluctuations over a range wider than the here obtained ΔE_{gp} values and hence much larger than ΔE_{gp}. The 3_{3+} cluster structure shows the lowest RMSD from the cluster crystal structure. All quantities were calculated using the NWChem computational chemistry package.[7]

structure	E_{gp} (eV)	ΔE_{gp} (eV)	ESE (eV)	RMSD (Å)
1_{3+}	-228581.87	0	1.45	0.283
2_{3+}	-228581.79	0.08	1.47	0.278
3_{3+}	-228581.74	0.13	1.47	0.258
4_{3+}	-228581.80	0.07	1.47	0.311
5_{3+}	-228581.76	0.11	1.48	0.279
6_{3+}	-228581.81	0.06	1.49	0.307

Table S12. Energy comparison of the optimized geometries of $[Fe_4S_4(SCH_3)_4]^{2-}$ (reduced cluster). We show energy quantities similar to those in Table S11, without comparing the $[Fe_4S_4]^{2+}$ structures to the crystal one, which is expected to correspond to an oxidized cluster.[8]

structure	E_{gp} (eV)	ΔE_{gp} (eV)	ESE (eV)
1_{2+}	-228581.81	0	4.84
2_{2+}	-228581.77	0.04	4.83
3_{2+}	-228581.78	0.03	4.82

Table S13. Mean value and standard deviation of the center-to-center distance for all relevant CT pairs over the MD snapshots obtained for the WT and Y345C proteins in complex with the nucleic acid duplex using the $\mathbf{A}_{3+}$ FF.

CT pair	WT protein complex	Y345C protein complex
$[Fe_4S_4]$-M307	16.30 ± 1.07	16.70 ± 0.69
$[Fe_4S_4]$-Y309	13.41 ± 0.31	13.38 ± 0.27
$[Fe_4S_4]$-DA7	19.21 ± 0.86	19.72 ± 0.44
M307-DA7	4.22 ± 0.45	4.15 ± 0.32
W327-M307	10.82 ± 0.87	10.21 ± 0.85
Y309-W327	6.63 ± 0.36	6.88 ± 0.32
Y309-M307	12.52 ± 0.36	12.36 ± 0.39
W327-DA7	11.77 ± 0.75	13.33 ± 0.45

Table S14. Mean value and standard deviation of the center-to-center distance for all relevant CT pairs over the MD snapshots obtained for the WT and Y345C proteins in complex with the nucleic acid duplex using the $\mathbf{3}_{3+}$ FF.

CT pair	WT protein complex	Y345C protein complex
$[Fe_4S_4]$-M307	16.98 ± 0.31	16.67 ± 0.57
$[Fe_4S_4]$-Y309	13.34 ± 0.21	13.38 ± 0.27
$[Fe_4S_4]$-DA7	19.75 ± 0.32	20.08 ± 0.47
M307-DA7	3.91 ± 0.27	4.29 ± 0.48
W327-M307	10.25 ± 0.46	10.22 ± 0.76
Y309-W327	6.50 ± 0.30	6.83 ± 0.32
Y309-M307	12.41 ± 0.30	12.37 ± 0.35
W327-DA7	12.36 ± 0.42	12.88 ± 0.76

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