

Supplementary Materials For

Theoretical Study of DNA Damage Recognition via Electron Transfer from the [4Fe-4S] Complex of MutY

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Free energy change and reorganization energy

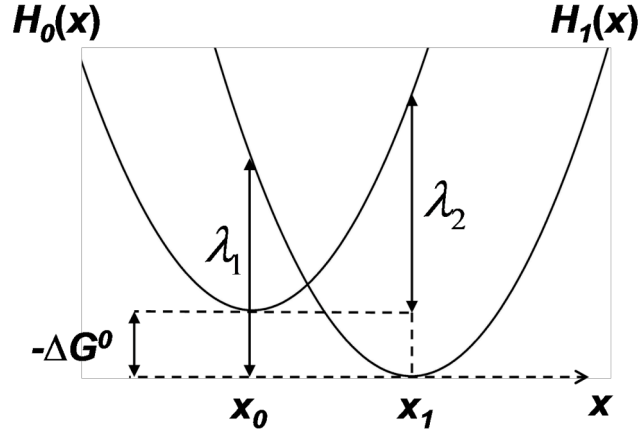


FIGURE S1. The energy H as a function of reaction coordinate x for the initial and final states.

As shown in Fig. S1, x_0 is the equilibrium reaction coordinate of the energy surface of the initial state (donor surface, $H_0(x)$), and x_1 is the equilibrium reaction coordinate of the energy surface of the final state (acceptor surface, $H_1(x)$). The energy difference between the donor surface and the acceptor surface at the initial coordinate x_0 is

$$h_1 = H_1(x_0) - H_0(x_0) = \lambda_1 - (-\Delta G^0), \quad (1)$$

where ΔG^0 is the free energy difference between the initial state and final state, and λ_1 is the reorganization energy for the relaxation from coordinate x_0 to coordinate x_1 for the acceptor surface after the transition from initial state to the final state. Similarly, the energy difference between the donor surface and the acceptor surface at the final coordinate x_1 is

$$h_2 = H_0(x_1) - H_1(x_1) = \lambda_2 + (-\Delta G^0), \quad (2)$$

where λ_2 is the reorganization energy for the relaxation from coordinate x_1 to coordinate x_0 for the donor surface if the system transits from the final state back to the initial state. If the donor surface and the acceptor surface are two parabolas with the same curvature, then $\lambda_1 = \lambda_2 = \lambda$. From equation (1) and (2), we can obtain the free energy difference $\Delta G^0 = \frac{1}{2}(h_1 - h_2)$, and the reorganization energy

$\lambda = \frac{1}{2}(h_1 + h_2)$. Since the Hamiltonian of the transition state can be expressed as $H(\eta) = (1 - \eta)H_0 + \eta H_1$, the derivative of H gives us the difference between H_1 and H_0 , i.e.,

$$\left. \frac{\partial H}{\partial \eta} \right|_{\eta=0} = H_1(\eta=0) - H_0(\eta=0) = h_1,$$

$$\left. \frac{\partial H}{\partial \eta} \right|_{\eta=1} = H_1(\eta=1) - H_0(\eta=1) = -h_2.$$

Hence ΔG^0 and λ can be obtained, given $\frac{\partial H}{\partial \eta}$ at the initial and final coordinates.

With the MutY-DNA complex divided into two parts containing the inner shell treated quantum mechanically, and the outer shell treated classically, the total energy can be expressed as

$$H = H_{all}^{MD} - H_D^{MD} - H_A^{MD} + H_D^{QM} + H_A^{QM},$$

where H_{all}^{MD} is the energy for the whole MutY-DNA complex calculated by MD simulation, H_D^{MD} , H_A^{MD} are the energies calculated by MD simulation for the donor and acceptor themselves, respectively, and H_D^{QM} , H_A^{QM} are the energies for the donor and acceptor obtained by quantum mechanical calculation. The energy difference at certain reaction coordinate x is then given by

$$\Delta H(x) = H_1(x) - H_0(x) = \Delta H_{all}^{MD}(x) - \Delta H_D^{MD}(x) - \Delta H_A^{MD}(x) + \Delta H_D^{QM}(x) + \Delta H_A^{QM}(x).$$

Therefore, the free energy change is

$$\Delta G^0 = \frac{1}{2}(\Delta H(x_0) + \Delta H(x_1)) = \Delta G_{all}^{0MD} - \Delta G_D^{0MD} - \Delta G_A^{0MD} + \Delta G_D^{0QM} + \Delta G_A^{0QM},$$

and the reorganization energy is given by

$$\lambda = \frac{1}{2}(\Delta H(x_0) - \Delta H(x_1)) = \lambda_{all}^{MD} - \lambda_D^{MD} - \lambda_A^{MD} + \lambda_D^{QM} + \lambda_A^{QM}.$$

Quantum mechanical calculation by SIESTA

The quantum mechanical calculations were carried out using the atomic-based density functional theory program SIESTA. It uses Troullier-Martins norm-conserving pseudopotentials (1) in the Kleinman-Bylander (2) form where we included nonlinear partial-core corrections for the Fe atom to take into account exchange and correlation effects in the core region (3). We used generalized gradient approximation (GGA) for the exchange-correlation energy functional with Perdew-Burke-Ernzerhof (PBE) parametrization (4). We used a double- ζ basis set (5) and included polarization orbitals for all atoms. To determine the minimum energy configuration within DFT, the system was allowed to relax till the force on each atom was less than 0.04 eV/Å. The quantum part of the donor in our calculation included the [4Fe-4S] cluster and the side chains (-S-CH₂-) of the four cysteine residues connected to the cluster. To be more specific, the system for quantum mechanical calculation is [Fe₄S₄(SCH₃)₄]^{2-/1-} cluster, where one hydrogen atom was added to each side chain in place of the C_α atom in the backbone as a terminal atom. The charges of the terminal H atoms were restrained such that when the terminal H atoms were removed and the cluster were embedded in the protein, the non-standard residue [Fe₄S₄(Cys)₄] could have integer charges. The values of ΔH_D^{QM} and ΔH_D^{MD} were both calculated for the [Fe₄S₄(SCH₃)₄]^{2-/1-} cluster, and the effect of the terminal atoms would cancel out in the evaluation of total energy difference ΔH . In addition, the spin of each Fe atom was set to high spin in the initial step in SIESTA calculation with two Fe atoms having opposite spin direction to the other two Fe atoms, which made low spin ground state for the cluster (S = 0 for the 2- charge state, and S = 1/2 for the 1- charge state), consistent with EPR data in experiments (6). The calculated net spin densities are ± 3.3 (in unit of 1/2) for each Fe in the 2- cluster, 3.4 and -3.1 for reduced and oxidized Fe, respectively, in the 1- cluster, which are consistent with those for high potential iron proteins (7).

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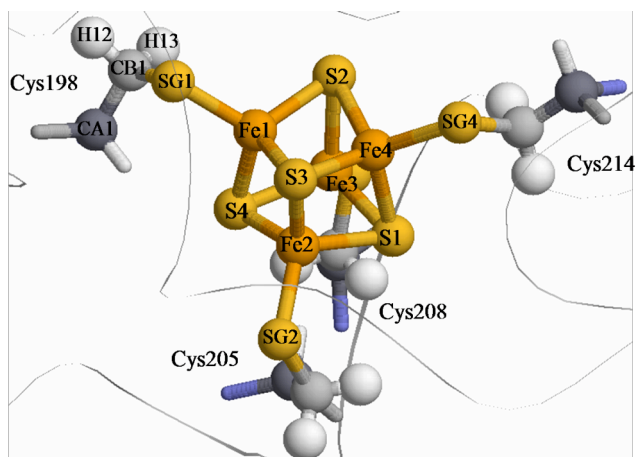


FIGURE S2. The structure of the [4Fe-4S] cluster in MutY.

TABLE S1. Calculated gas-phase oxidation potential (in eV) of DNA nucleobases and iron-sulfur cluster using SIESTA

System	SIESTA	Exp ^a	Ref. 34 ^b
G	7.71	7.77	7.68
A	8.11	8.26	8.09
C	8.55	8.68	8.56
T	8.70	8.87	8.71
OxoG	7.45	-	7.39
$[\text{Fe}_4\text{S}_4(\text{SCH}_3)_4]^{2-}$	-0.12 (0.03 ^c)	-	-

^a Experimental data taken from V. M. Orlov et al., Tetrahedron Lett. 1976, 48, 4377.

^b Calculated values taken from Ref. 34.

^c The number in parentheses is calculated value taken from Ref. 32.

TABLE S2. The value of $\log_{10} k_{et}$ in MutY and DNA complex.

System	S(Cys198)-A17	Fe-A17	S(Cys198)-C16	Fe-C16
MutY-DNA (MD)	7.542±0.3	6.235±0.3	3.598±0.714	2.245±0.714
L154F-DNA (MD)	7.338±0.302	5.983±0.302	-	-