

Effects of local electric fields on the redox free energy of single stranded DNA

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Supporting Information

Theory

Defining with \mathbf{r}_n the nuclear coordinates of the QC and \mathbf{x} the coordinates of the atoms providing the (classical) perturbing field we can write the QC (electronic) Hamiltonian matrix (i.e. the matrix expressing the Hamiltonian operator) as [1, 2, 3, 4]

$$\begin{aligned}\widetilde{H} &= \widetilde{H}^0(\mathbf{r}_n) + \widetilde{V}(\mathbf{r}_0, \mathbf{x}) \\ &\cong \widetilde{H}^0(\mathbf{r}_n) + q_T \mathcal{V}(\mathbf{r}_0, \mathbf{x}) \widetilde{I} + \widetilde{Z}_1(\mathbf{E}(\mathbf{r}_0, \mathbf{x}), \mathbf{r}_n) + \Delta V(\mathbf{r}_n, \mathbf{x}) \widetilde{I}\end{aligned}\quad (1)$$

where q_T is the QC total charge, $\mathcal{V}(\mathbf{r}_0, \mathbf{x})$ and $\mathbf{E}(\mathbf{r}_0, \mathbf{x})$ are the (perturbing) electric potential and electric field, as provided by the environment atomic charges, at a given QC \mathbf{r}_0 position (typically the mass center), $\widetilde{Z}_1(\mathbf{E}, \mathbf{r}_n)$ is the perturbation energy matrix explicitly given by $[\widetilde{Z}_1]_{l,l'} = -\mathbf{E} \cdot \langle \Phi_l^0 | \hat{\boldsymbol{\mu}} | \Phi_{l'}^0 \rangle$ with $\hat{\boldsymbol{\mu}}$ the dipole operator, and $\Delta V(\mathbf{r}_n, \mathbf{x})$ approximates all the higher order terms as a short range potential (note that in the case the quantum center is a subpart of a molecule ΔV may also include an additive constant corresponding to a possible reference energy shift). The previous equation providing the QC perturbed Hamiltonian matrix \widetilde{H} for a quantum center interacting with a semi-classical atomic-molecular environment, may be equivalently expressed in the typical operator notation

$$\begin{aligned}\hat{H} &= \hat{H}^0 + \hat{V} \\ &\cong \hat{H}^0 + q_T \mathcal{V} - \mathbf{E} \cdot \hat{\boldsymbol{\mu}} + \Delta V\end{aligned}\quad (2)$$

with the perturbation operator \hat{V} physically corresponding to the perturbation due to the ground state environment atomic-molecular field acting on the QC. The eigenvectors of \widetilde{H} , i.e. the eigenstates of \hat{H} , can be used to obtain the perturbed QC electronic properties for each QC perturbed state at each atomic

configuration as provided by any sampling method, e.g. MD simulations. Note that we may combine PMM calculations, providing the perturbed electronic energies and properties, with statistical mechanical derivations in order to obtain the free energy variation due to QC state transitions [2, 3, 5, 6, 7, 8]. For a charge transfer reaction, the case of interest in the present paper and previously investigated for simpler systems [9, 10, 11], we may express the free energy change due to charging the QC as

$$\Delta A = -k_B T \ln \langle e^{-\beta \Delta \mathcal{U}'} \rangle \cong -k_B T \ln \langle e^{-\beta \Delta(\epsilon' + q_T \mathcal{V})} \rangle \quad (3)$$

where $\Delta \mathcal{U}'$ is the energy variation of the whole system due to QC charging, $\Delta(\epsilon' + q_T \mathcal{V})$ the corresponding change of QC perturbed ground state energy when disregarding quantum vibrational energy and short range potential[3], (ϵ' is the ground state eigenvalue of \tilde{Z}_1) and the average is typically taken in the uncharged QC ensemble (note that for a charging process no relevant change of the vibrational partition function and atomic short range potential is expected and in usual MD atomistic force-field no atomic polarization beyond the pair additive dispersion interaction is considered and hence the environment internal energy is unchanged for any QC state transition). For a single stranded DNA molecule made of n bases we may therefore express the free energy change for the l -th base charging $B_l \rightarrow B_l^\pm$, $l = 1, n$ via

$$\begin{aligned} \Delta A_{B_l \rightarrow B_l^\pm} &= -k_B T \ln \left\langle e^{-\beta \Delta \mathcal{U}'_{B_l \rightarrow B_l^\pm}} \right\rangle_{B_l} \\ &\cong -k_B T \ln \left\langle e^{-\beta \Delta(\epsilon' + q_T \mathcal{V})_{B_l \rightarrow B_l^\pm}} \right\rangle_{B_l} \end{aligned} \quad (4)$$

Computational methods

Quantum mechanical calculations, providing the unperturbed properties of the Quantum Center (the nucleobase), were performed by means of the Density Functional Theory (DFT), using the B3LYP functional, as implemented in the Gaussian Software package[12]. All the structure were relaxed and, then, the excited properties needed to run the PMM procedure were calculated by using Time-Dependent DFT. Although the aim of this work is to address the effects of the environment (the rest of the single strand and the applied external electric fields) on the reduction/oxidation free energies, our unperturbed results, i.e. nucleobases ionization potentials and electronic affinities, were compared with recent experimental and theoretical data: the relative order of ionization energies is consistent with previous experiments (see Crespo-Hernandez[13] and references therein) and our calculated (unperturbed) electron affinities are in line with the data reported by Wesolowski et al.[14].

Molecular dynamics simulations were performed by using Gromacs software[15]. Each DNA sequence was thermalized and equilibrated for 10 ns. Then, MD tra-

Table 1: Nucleobase redox free energies and their fluctuations (within parenthesis) along the 140-mer. To remove border effects, all the data were calculated considering only the (124) central nucleobases.

Redox Free Energies and fluctuations (kJ/mol)		
Adenine	Reduction	969 (68)
	Oxidation	-175 (40)
Cytosine	Reduction	952 (40)
	Oxidation	-135 (32)
Guanine	Reduction	826 (67)
	Oxidation	-248 (35)
Thymine	Reduction	936 (33)
	Oxidation	-126 (37)

jectories of 100 ns were produced with a time step of 2 fs in the NVT ensemble and all the bond lengths were kept fixed at their equilibrium distance via LINCS algorithm[16]. To take into account of the vacuo conditions, the simulations were performed without cut-off and the atomic charges were slightly modified as proposed by Rueda et al.[17].

0.1 Additional Sequence

To assure that redox properties of the four nucleobase are constant within a DNA-strand, we calculated the reduction and oxidation potentials of 140 nucleobases extracted from the single-stranded M13mp18 DNA molecule (starting from nucleotide 5320). Results shown in Table I indicate that the value of $\Delta A_{red/ox}$ only depends on the nucleobase type and, hence, the data presented in the main article might hold for different DNA sequences. It is worth noting that the absolute values of $\Delta A_{red/ox}$ do depend on the strand length, as longer is the DNA molecule, larger is the electric field felt by each nucleobase.

References

- [1] R. Spezia, M. Aschi, A. Di Nola, and A. Amadei. Extension of the perturbed matrix method: application to a water molecule. *Chem. Phys. Lett.*, 365:450–456, 2002.
- [2] A. Amadei, M. D’Abramo, C. Zazza, and M. Aschi. Electronic properties of formaldehyde: a theoretical study. *Chem. Phys. Lett.*, 381:187–193, 2003.

- [3] A. Amadei, M. D'Alessandro, and M. Aschi. Statistical mechanical modeling of chemical reactions in complex systems: the reaction free energy surface. *J. Phys. Chem. B*, 108:16250–16254, 2004.
- [4] A. Amadei, F. Marinelli, M. D'Abramo, M. D'Alessandro, M. Anselmi, A. Di Nola, and M. Aschi. Theoretical modeling of vibro-electronic quantum states in complex molecular systems: solvated carbon monoxide, a test case. *J. Chem. Phys.*, 122:124506, 2005.
- [5] M. D'Alessandro, F. Marinelli, M. D'Abramo, M. Aschi, A. Di Nola, and A. Amadei. Ground and excited electronic state thermodynamics of aqueous carbon monoxide: a theoretical study. *J. Chem. Phys.*, 122:124507, 2005.
- [6] M. D'Alessandro, M. Aschi, M. Paci, A. Di Nola, and A. Amadei. Theoretical modeling of enzyme reactions chemistry: the electron transfer of the reduction mechanism in CuZn superoxide dismutase. *J. Phys. Chem. B*, 108:16255–16260, 2004.
- [7] M. Aschi, M. D'Abramo, F. Ramondo, I. Daidone, M. D'Alessandro, A. Di Nola, and A. Amadei. Theoretical modeling of chemical reactions in complex environments: The intramolecular proton transfer in aqueous malonaldehyde. *J. Phys. Org. Chem.*, 19:518–530, 2006.
- [8] A. Amadei, M. D'Abramo, I. Daidone, M. D'Alessandro, A. Di Nola, and M. Aschi. Statistical mechanical modelling of chemical reactions in complex systems: the kinetics of the haem carbon monoxide binding-unbinding reaction in myoglobin. *Theor. Chem. Acc.*, 117:637–647, 2007.
- [9] M. Aschi, C. Di Teodoro, A. Amadei, D. Roccatano, F. Malatesta, and L. Ottaviano. Conformational and electronic properties of a microperoxidase in aqueous solution: a computational study. *ChemPhysChem*, 6:681–689, 2005.
- [10] M. Aschi, M. D'Alessandro, M. Pellegrino, A. Di Nola, M. D'Abramo, and A. Amadei. Intramolecular charge transfer in π -conjugated oligomers: a theoretical study on the effect of temperature and oxidation state. *Theor. Chem. Acc.*, 119(5-6):469–476, 2008.
- [11] Costantino Zazza, Andrea Amadei, Nico Sanna, and Massimiliano Aschi. Can a synthetic thread act as an electrochemically switchable molecular device? *Chem. Commun.*, (29):3399–3401, Aug 2008.
- [12] M.J. Frisch et al. Gaussian 03, Revision C.02. Gaussian, Inc., Wallingford, CT, 2004.

- [13] C. E. Crespo-Hernandez, R. Arce, Y. Ishikawa, L. Gorb, J. Leszczynski, and David M. Close. Ab initio ionization energy thresholds of dna and rna bases in gas phase and in aqueous solution. *J. Phys. Chem. A*, 108 (30):6373–6377, 2004.
- [14] S. Wesolowski, M.L. Leininger, P.N. Pentchev, and H.F. Schaefer III. *J. Am. Chem. Soc.*, 17:123, 2001.
- [15] D. van der Spoel, E. Lindahl, B. Hess, G. Groenhof, A. E. Mark, and H. J. C. Berendsen. Gromacs: Fast, flexible and free. *J. Comp. Chem.*, 26:1701–1718, 2005.
- [16] B. Hess, H. Bekker, H. J. C. Berendsen, and J. G. E. M. Fraaije. LINCS: A Linear Constraint Solver for Molecular Simulation. *J. Comput. Chem.*, 18:1463, 1997.
- [17] Manuel Rueda, Susana G Kalko, F. Javier Luque, and Modesto Orozco. The structure and dynamics of dna in the gas phase. *J Am Chem Soc*, 125(26):8007–8014, Jul 2003.