Auxiliary Material to: The persistence of structure over fluctuations in biological electron-transfer reactions

Ilya A. Balabin and David N. Beratan
Department of Chemistry, Duke University, Durham, NC 27708

Spiros S. Skourtis
Department of Physics, University of Cyprus, 1678 Nicosia, Cyprus
(Dated: September 5, 2008)

Molecular dynamics simulations

All simulated systems were solvated in a box of TIP3 water [1], and sodium and chloride counterions were added to ionic concentration of $0.05-0.1$ M to neutralize the protein charges. Each system underwent $100-500$ minimization steps and $200-500$ ps of equilibration, followed by 100 ps (for unimolecular reactions) or 150 ps (for bimolecular reactions) of molecular dynamics (MD) simulations at 310 K. Simulations used the NpT ensemble, 1 fs time step, the *Charmm* [2] or *Amber* [3] forcefields, periodic boundary conditions, and particle-mesh Ewald full electrostatics calculations [4, 5]. A conformation was saved every 1 ps, generating 100 snapshots for each ruthenated protein and 150 snapshots for each water-mediated system.

Washing out structural electronic coupling disorder by thermal fluctuations

Fig. 1 shows a schematic diagram of the two distinct disorder regimes. Washing out of structural disorder by dynamical disorder would cause the widths of the $P_\gamma(T_{DA})$ distributions to become large at large donor-acceptor separations ($R_{DA} \gg R_c$). The resulting significant overlap among the $P_\gamma(T_{DA})$ functions would cause different species to have similar $\langle T_{DA}^2 \rangle$ (Fig. 1b).

Significance of the tunneling coupling fluctuations

Contributions of the average coupling $\langle T_{DA} \rangle$ and the variance σ to the mean square coupling $\langle T_{DA}^2 \rangle$ are shown in Figure 2. In both protein-mediated and water-mediated reactions, the average coupling dominates at shorter distances, while fluctuations control tunneling at longer distances. The transition distance R_c for equal relative contributions was estimated as the crossing point in the linear regressions of $\langle T_{DA} \rangle^2$ and σ^2. For water, the correlation coefficients in the linear regression were in the range -0.95 to -0.96, and the estimate for R_c was 3.1 ± 0.8 Å. For proteins, structural variations resulted in considerably smaller but still significant correlations of -0.71 to -0.73, and the estimate for R_c was about 7

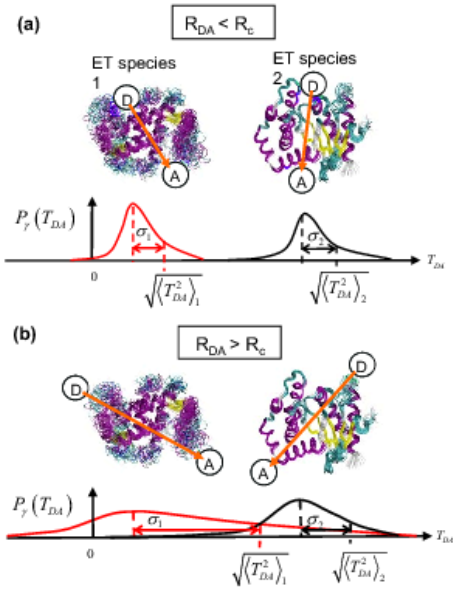

FIG. 1: T_{DA} probability density function for pairs of ET species at different R_{DA} values. (a) The limit of strong structural disorder for $R_{DA} < R_c$ ($S = (\langle T_{DA}^2 \rangle_2 - \langle T_{DA}^2 \rangle_1)/(\langle T_{DA}^2 \rangle_2 + \langle T_{DA}^2 \rangle_1) \sim 1$) . (b) The limit of weak structural disorder for $R_{DA} > R_c$ ($S \ll 1$). The T_{DA} axis scale for $R_{DA} > R_c$ (b) is smaller than the scale for $R_{DA} < R_c$ (a).

Å. Errors for this estimate are large, since the crossing point was well outside of the tunneling distance range in the studied proteins. In addition, protein structural diversity leads to significant variation of the tunneling coupling dependence on distance, and specific proteins need not follow this trend. For example, azurin derivative $H122$ has a mean square coupling nearly dominated by σ^2, while azurin derivative 124 at longer distance is dominated by $\langle T_{DA} \rangle^2$.

Correlations of the thermal atomic motion

Figure 3 shows the distance dependences of the thermal atomic motion correlation κ_{ij} for wild type azurin and its water environment. At zero distance, the correlation between thermal motion of an atom and itself yields $\kappa_{ii} = 1$. As the distance increases, κ_{ij} first decays nearly

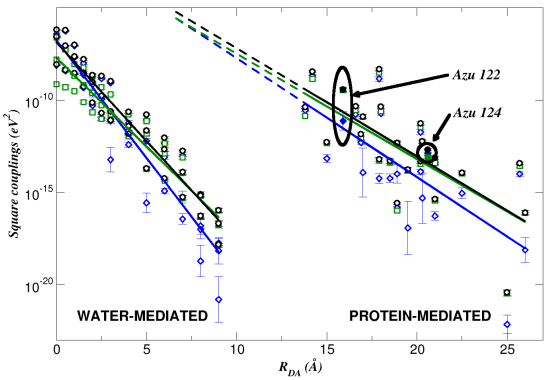

FIG. 2: Contributions from the average coupling ($\langle T_{DA}\rangle^2$, blue diamonds) and the coupling variance (σ^2, green squares) to the mean square coupling ($\langle T_{DA}^2\rangle$, black circles)) as functions of tunneling distance. Water-mediated reactions correspond to the distance range of $0-9$ Å (between porphyrin rings), and protein-mediated reactions correspond to the distance range of $13-26$ Å (metal-to-metal). The least square fit to each contribution is shown with a solid line, and the dashed lines show extensions of the least square fits for proteins to the cross-over point.

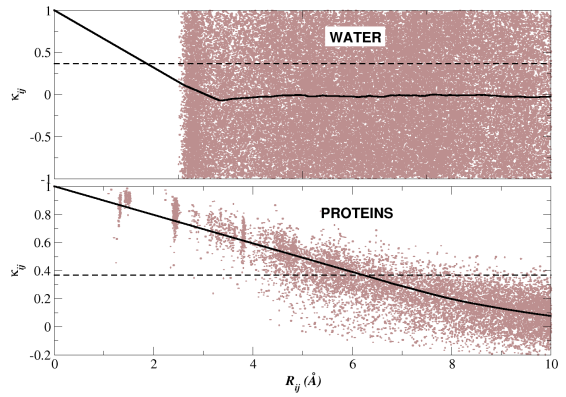

FIG. 3: Correlations of thermal atomic motions in water (top panel) and proteins (lower panel). The water data start at about 2.5 Å, which is the shortest distance between two oxygen atoms. The high mobility of water molecules leads to a rapid loss of correlation with distance and a broad distribution of correlations for any specific distance. The banded structure of the protein data at shorter distances arises from the fixed distances between nearest-neighbor and second-neighbor protein backbone atoms. The transition distance is 1.9 ± 0.5 Å for water and 6.2 ± 1.4 Å for proteins. The solid lines show running averages calculated over $20,000$ data points, and the dashed lines indicate the value of $1/e$ that defines the transition distance.

exponentially and then fluctuates randomly around zero (Fig. 3). The transition distance at which $\kappa_{ij}=1/e$ was estimated as 1.9 ± 0.5 for water and 6.2 ± 1.4 Å for proteins. The estimates were based on running averages calculated over $20,000$ data points, because the transition distance in water is shorter than the closest distance between any two oxygen atoms (~ 2.5 Å). Variation of the running average window width had no significant effect on the results in the range of $100-20,000$ data points. The transition distances were remarkably robust to changes in temperature in the range of $30-310$ K, protein secondary structure (calculations for adenylate kinase yielded nearly identical results) and the distance to the protein surface in the case of water ($2-7$ Å).

[1] W. L. Jorgensen, J. Chandrasekhar, J. Madura, R. W. Impey, and M. L. Klein, J. Chem. Phys. **79**, 926 (1983).

[2] A. D. Mackerell, D. Bashford, M. Bellott, R. L. Dunbrack, J. D. Evanseck, M. J. Field, S. Fischer, J. Gao, H. Guo, S. Ha, et al., J. Phys. Chem. B **102**, 3586 (1998).

[3] D. A. Case, T. E. Cheatham, T. Darden, H. Gohlke, R. Luo, K. M. Merz, A. Onufriev, C. Simmerling, B. Wang, and R. Woods, J. Comp. Chem. **26**, 1668 (2005).

[4] S. S. Skourtis, I. A. Balabin, T. Kawatsu, and D. N. Beratan, Proc. Natl. Acad. Sci. USA **102**, 3552 (2005).

[5] J. Lin, I. A. Balabin, and D. N. Beratan, Science **310**, 1311 (2005).