

Molecular Orientation Effects on the Rates of Heterogeneous Electron Transfer of Unsymmetric Dendrimers

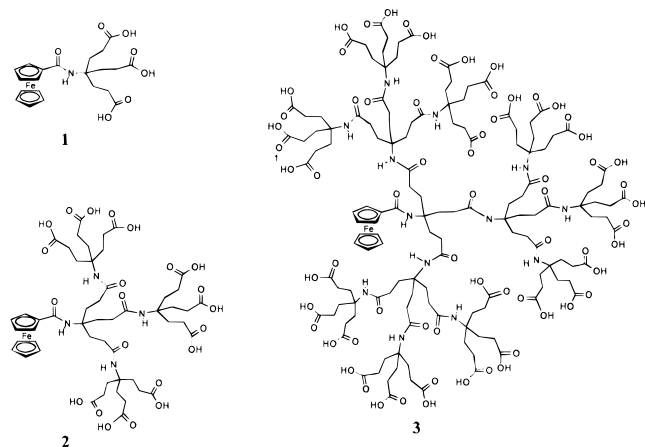
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Redox proteins often have their prosthetic groups unsymmetrically located and partially buried in the protein's polypeptide backbone. In electrochemical experiments, the interfacial orientation of the protein near the electrode surface influences the effective rates of the heterogeneous electron transfer (*et*) reactions.¹ Cytochrome *c* affords an excellent and clear example of these phenomena.² In this communication, we describe similar orientation-dependent, heterogeneous *et* rates involving, for the first time, fully synthetic redox active systems. Interfacial orientations and rates of heterogeneous *et* in these dendrimer systems can be reversibly controlled through pH changes.

We have previously reported the preparation and electrochemistry of dendrimers containing a single ferrocene subunit positioned unsymmetrically "off center" in the dendrimer structure.³ Hydrolysis of the peripheral *tert*-butyl esters in these dendrimers yields the corresponding water-soluble, carboxylic acid dendrimers **1–3** (see Supporting Information). From pH titration data we have found that the p*K*_a of the carboxylic acids in these dendrimers is in the range 4.5–6 (Supporting Information). Therefore, at pH ≥ 7 compounds **1–3** are fully ionized and have multiple negative charges. These charges can be utilized to orient the dendrimers at the electrode–solution interface.



Initially, we surveyed the electrochemistry of **1–3** in 0.1 M NaCl aqueous solution, using gold beads⁴ as working electrodes. The voltammetric response [cyclic voltammetry (CV) and square wave voltammetry (SWV)] in the anodic potential window

(1) (a) Guo, L.-H.; Hill, H. A. O. *Adv. Inorg. Chem.* **1991**, *36*, 341. (b) *Redox Chemistry and Interfacial Behavior of Biological Molecules*; Dryhurst, G., Niki, K., Eds.; New York: Plenum, 1988. (c) Kong, J.; Lu, Z.; Lvov, Y. M.; Desamero, R. Z. B.; Frank, H. A.; Rusling, J. F. *J. Am. Chem. Soc.* **1998**, *120*, 7371.

(2) (a) Kasmi, A. E.; Wallace, J. M.; Bowden, E. F.; Binet, S. M.; Linderman, R. J. *J. Am. Chem. Soc.* **1998**, *120*, 225. (b) Taniuchi, I. *Electrochem. Soc. Interface* **1997**, *4*(6), 34. (c) Bowden, E. F. *Electrochem. Soc. Interface* **1997**, *4*(6), 40. (d) Bowden, E. F.; Hawkridge, F. M.; Blount, H. N. In *Comprehensive Treatise of Electrochemistry*; Srinivasan, S., Chizmadzhev, Y. A., Bockris, J. O'M., Conway, B. E., Yeager, E., Eds.; New York: Plenum, 1985; Vol. 10, p 297.

(3) Cardona, C. M.; Kaifer, A. E. *J. Am. Chem. Soc.* **1998**, *120*, 4023.

(4) The procedures for the preparation of these electrodes have been described before: Gómez, M.; Li, J.; Kaifer, A. E. *Langmuir* **1991**, *7*, 1797.

Table 1. Electrochemical Parameters for Dendrimers **1–3** at 25 °C
Bare Gold Electrodes (0.1 M NaCl)

dendrimer	$E_{1/2}$ (V vs SSCE)	D_0 (cm ² /s)	α	k^0 (cm/s) ^a
1	0.356	$(1.1 \pm 0.1) \times 10^{-5}$	0.5	0.10 ± 0.04
2	0.386	$(4.5 \pm 0.3) \times 10^{-6}$	0.5	0.01 ± 0.002
3	0.400	$(3.0 \pm 0.2) \times 10^{-6}$	0.4	0.004 ± 0.0005
Cystamine-Covered Au Electrodes				
dendrimer	pH	k^0 (cm/s)		
1	4.0	0.10 ± 0.04		
1	7.0	0.08 ± 0.02		
2	4.2	$(8.0 \pm 1.0) \times 10^{-3}$		
2	5.3	$(1.3 \pm 0.1) \times 10^{-3}$		
2	6.0	$(5.8 \pm 0.1) \times 10^{-4}$		
2	7.0	$(1.5 \pm 0.1) \times 10^{-5}$		
3	3.0	$(2.0 \pm 0.2) \times 10^{-3}$		
3	4.2	$(6.0 \pm 0.1) \times 10^{-4}$		
3	5.4	$(8.0 \pm 0.1) \times 10^{-5}$		
3	7.4	$(6.0 \pm 0.1) \times 10^{-6}$		

^a These values were found to be insensitive to the solution pH in the range 3–7.

necessary to drive the one-electron oxidation of the ferrocene residue was found to be pH-independent and diffusion-controlled (Supporting Information), as is normally the case with ferrocene derivatives.⁵ We used digital simulations⁶ of the SWV data to determine the relevant electrochemical parameters (Table 1). No significant differences were observed between the voltammograms recorded at solution pH values of 3 and 7. As the charges on any of these dendrimers are quite different at these two pH values, we conclude that the charge density at the electrode surface⁷ is not sufficiently large to affect the average orientation of the dendrimer at the electrode–solution interface under our experimental conditions.

To increase the surface charge density on the gold electrodes we resorted to their derivatization with thiolate monolayers of positively charged amines. The monolayers were deposited on the gold electrodes by exposing them to cystamine dihydrochloride aqueous solutions.⁸ The surface-immobilized amines exhibit a p*K*_a > 7 and remain protonated throughout our experiments in the pH range 3–7.⁹ Interestingly, the electrochemical response of dendrimers **2** and **3** on cystamine-covered electrodes was found to be extremely pH-dependent. For instance, Figure 1A shows the SWV response of a 0.1 mM solution of **2** at pH 4.2. Digital simulations of this voltammetric response reveal relatively fast heterogeneous *et* kinetics¹⁰ ($k^0 = 0.008$ cm/s). When the pH increases the voltammetric response reflects gradually slower *et* kinetics (see parts B and C of Figure 1) as the dendrimer's carboxylic acid groups undergo ionization and acquire negative charge. At pH 7, the voltammetric response of the dendrimer is so slow ($k^0 = 1.5 \times 10^{-5}$ cm/s) that the ferrocene oxidation peak

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(6) We used the ESP simulation package that is available (Dr. Carlo Nervi, University of Torino, Italy) on the Internet at: <http://lem.ch.unito.it/chemistry/electrochemistry.html>.

(7) At the potentials necessary to drive the oxidation of ferrocene, the charge density on the electrode surface is likely to be positive, i.e., the potentials are larger than the corresponding potential of zero charge (pzc). See, for instance: Hamelin, A.; Lecoeur, J. *Collect. Czech Chem. Commun.* **1971**, *36*, 714.

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(9) Sun, L.; Johnson, B.; Wade, T.; Crooks, R. M. *J. Phys. Chem.* **1990**, *94*, 8869.

(10) Due to the electrostatic effects involved in these measurements, we must note that the reported k^0 values are *apparent rate constants*, as they depend on the supporting electrolyte concentration used in these experiments.

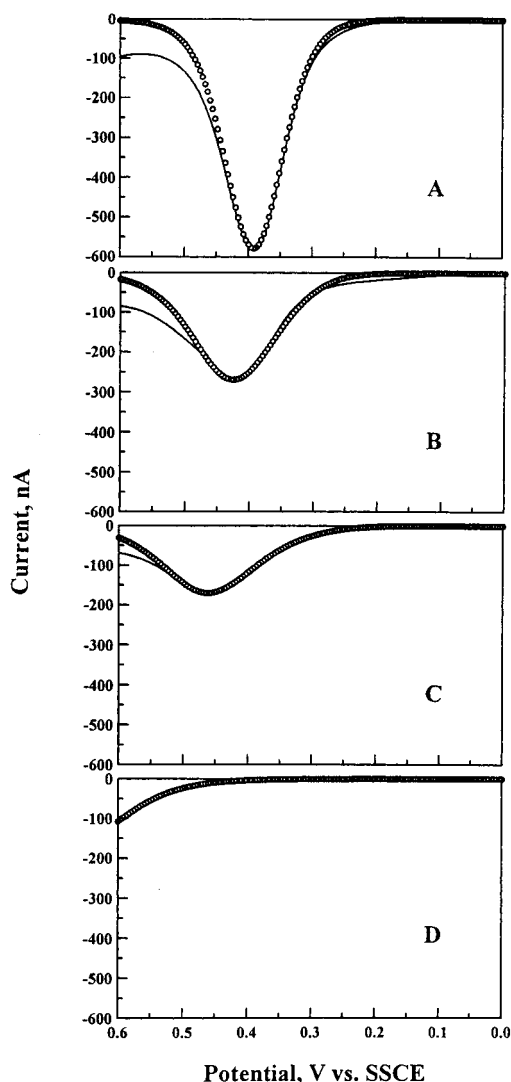
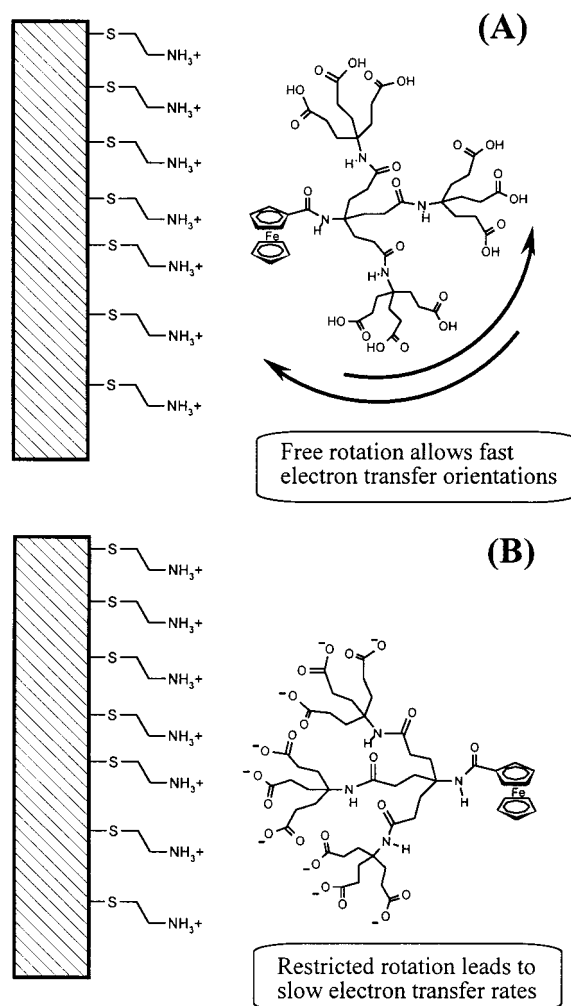


Figure 1. Experimental (after background subtraction, continuous line) and simulated (circles) SWV responses of a cystamine-covered gold bead electrode (0.018 cm^2) immersed in a 0.1 mM $2/0.1 \text{ M}$ NaCl aqueous solution. The pH was adjusted by addition of HCl or NaOH to the following values: (A) 4.2, (B) 5.3, (C) 6.0, and (D) 7.0. SWV parameters: potential step, 4 mV ; pulse amplitude, 25 mV ; frequency, 15 Hz .

is essentially not observed (Figure 1D). Dendrimer **3** behaves in a very similar fashion. These pH effects on the k^o value for the one-electron oxidation of dendrimers **2** and **3** (Table 1) are completely reversible, reproducible, and cannot be rationalized using double-layer effects. In striking contrast with **2** and **3**, the voltammetric behavior of compound **1** on cystamine-covered gold electrodes does not exhibit any significant pH effects in the surveyed range (Table 1).

In the range of pH values examined the cystamine monolayer always remains positively charged, while the charge on the dendrimers can be controlled from zero (at low pH) to large negative values (at neutral pH). The electrochemical data reported here clearly indicate that, at low pH, the uncharged dendrimers can adopt any orientation as they approach the monolayer-solution interface, including those in which the ferrocene subunit faces the electrode, yielding relatively fast *et* rates. At higher pH values, the negatively charged dendrimers approach the interface with the negative charges facing the positively charged monolayer (Scheme 1). The electrostatic interactions restrict molecular rotation, leading to interfacial dendrimer orientations in which the distance between the ferrocene residue and the electrode surface is maximized and resulting in very slow heterogeneous *et* rates.¹¹ The magnitude of these effects is of course strongly

Scheme 1. Interfacial Orientation of Dendrimer 2



dependent on the molecular size of the dendrimers. Thus, no significant effects are observed with **1**, while **2** and **3** exhibit strongly pH-dependent electrochemical behavior. The electrostatic nature of the forces restricting the rotation of these dendrimers at neutral pH can be further verified by changing the concentration of supporting electrolyte in the solution. When we increased the NaCl concentration from 0.1 to 1.0 M in the electrode-solution system represented in Figure 1D, Coulombic charge screening effects become significant, decreasing the attractive forces between the monolayer and the dendrimer, increasing the dendrimer's freedom of rotation, and giving rise to faster *et* rates.

To the best of our knowledge these results constitute the first example of strong orientational effects on the heterogeneous *et* rates of completely artificial (synthetic) compounds. The electrochemical behavior described here adds to the general similarities between these unsymmetric redox active dendrimers and some redox proteins.

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Supporting Information Available: The synthetic procedure for the preparation of dendrimer **2**, experimental details on the electrochemical experiments and data analysis, pH titration data, and changes in the voltammetric behavior caused by increasing concentration of supporting electrolyte (PDF). This material is available free of charge via the Internet at <http://pubs.acs.org>.

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(11) For a related report concerning SAM manipulations to exert reversible control on the *et* reactions of cytochrome *c*, see: Lion-Dagan, M.; Katz, E.; Willner, I. *J. Chem. Soc., Chem. Commun.* **1994**, 2741.