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# Aggregation of Ferrocene Pendant Groups along the Backbone of DNA for a Supramolecular Redox System

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***Abstract:*** *Redox-active ferrocenes bearing a long alkylene chain (FUT) were aggregated along the backbone of double helical DNA to afford redox-active (outer) and hydrophobic (inner) spheres around the double helical core. In this system, the redox potential of the ferrocene moiety shifted anodically, compared with the uncomplexed FUT, possibly due to hydrophobic interaction between the long alkylene chains.* © 1998 Elsevier Science Ltd. All rights reserved.

An efficient redox system of transition metal complexes is essential to develop versatile materials and catalytic redox reactions. Ferrocenes have attracted much attention in their application to materials due to a reversible redox couple and rotatory cyclopentadienyl rings.[1] We have already focused on such properties to demonstrate a unique coordination behavior of the ferrocene ligands bearing podand *N*-heterocyclic pendant groups.[2] Controlled arrangement of redox-active moieties is considered to be a convenient approach to modulate the redox properties. Biomolecules are known to exist in a highly-ordered structure to fulfill the specific function as observed in the double helix of DNA or α-helix and β-sheet of peptides. The introduction of redox-active complexes into such highly-ordered biomolecules is envisioned to provide new biomaterials or efficient redox systems.[3] We herein report the construction of a supramolecular redox system by aggregating the redox-active ferrocene function along the backbone of DNA.

Treatment of salmon sperm DNA with 0.05 equiv of (11-ferrocenyl)undecyltrimethylammonium bromide (FUT) to the phosphate anions of DNA in a HEPES buffer solution (pH 8.0) at room temperature afforded the FUT-DNA (1/20) complex **1**, which is soluble in the buffer solution. The formation of the complex is confirmed by the following observations. It should be noted that the redox waves of **1** shifted anodically ($E_{1/2}$: **1**, 140 mV; FUT, 113 mV *vs* SCE; [FUT] = 1.0 x $10^{-3}$ M; HEPES buffer) in the cyclic voltammograms.[4] Although the anodic shift was found to depend on the concentration of FUT or the complex **1** in a HEPES buffer solution as shown in Figure 1, the complexation enhanced the anodic shift even at lower concentration of the FUT unit as compared with the uncomplexed FUT.[5] From these results, FUT units are considered to be aggregated cooperatively and in closer contact along the minor groove of DNA in the case of


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the complex **1** (Scheme 1). As a result, the hydrophobic chains are presumed to compact more tightly, increasing the interactions of neighboring ferrocene groups. As one of the ferrocene groups becomes oxidized, the ability of other ferrocene groups to be oxidized apparently becomes more difficult, resulting in the above-mentioned anodic shift. Also, the redox reversibility of **1** suggests that the structure is maintained even in the oxidized form.

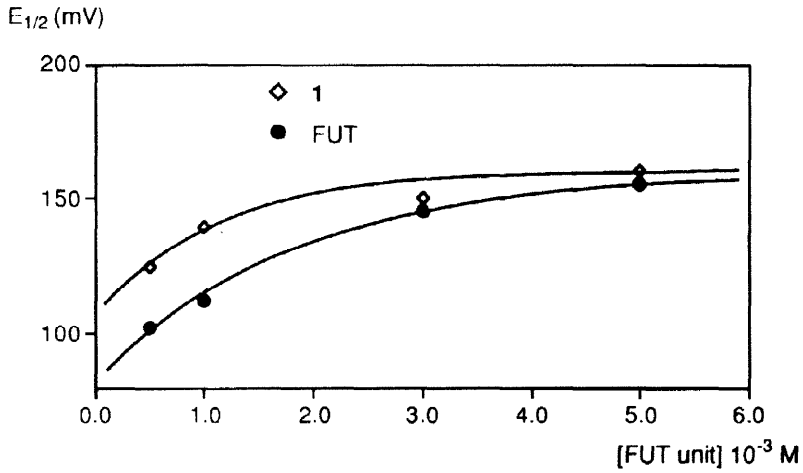
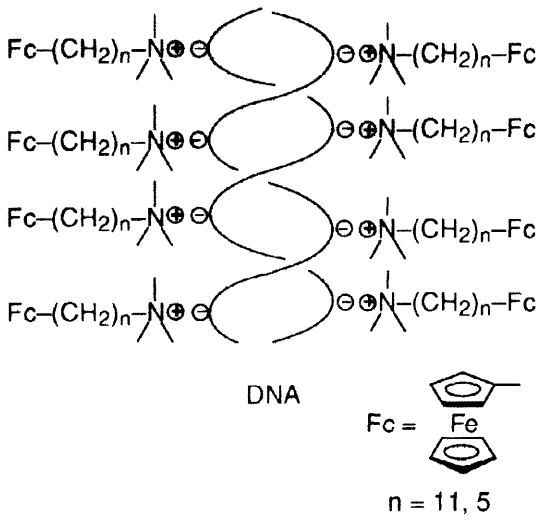



**Figure 1.** Comparison of $E_{1/2}$ of FUT (filled circles) and **1** (empty diamonds) in variable concentration of FUT unit.




Scheme 1.

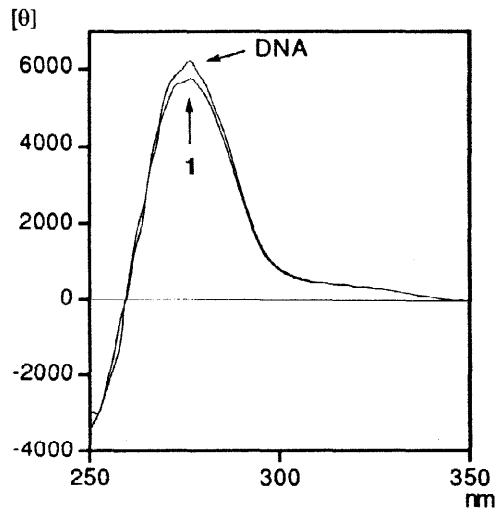



**Figure 2.** CD spectra of **1** and salmon sperm DNA in a HEPES buffer solution (pH 8.0, [DNA] = 50 μM bp, 30 °C)

Such an effect strongly depends on the chain length as expected. No distinct shift of the redox potential was observed in the case of (5-ferrocenyl)pentyltrimethylammonium bromide (FPT) and the FPT-DNA complex **2** formed similarly or with even a stoichiometric equivalent of FPT, where the alkylene chain of FPT is not long enough to provide an increased interaction of the ferrocene groups. These results are also consistent with the hydrophobic interaction of FUT chains and the lack of direct interaction between DNA and the ferrocene moieties.

Such a complexation was also supported by spectral data. The CD spectrum, which was measured in a HEPES buffer solution, was almost identical to that of uncomplexed DNA (Figure 2). Neither distinct bathochromism nor hypochromism was observed in UV-vis spectra. These findings indicate that the DNA does not unwind upon FUT binding. It is not likely that the ferrocene would intercalate since most known intercalators tend to be flat polyaromatic compounds or planar inorganic complexes, but outside binding of FUT to DNA occurs without change of the helical structure.

Increase in the amount of FUT to a stoichiometric equivalent to the phosphate anions of DNA resulted in the formation of the complex **3**[6] as an insoluble precipitate in a buffer solution, possibly due to the formation of a hydrophobic core of the alkylene chains. Of interest is that the isolated complex was soluble in organic solvent like DMF and DMSO as reported in a DNA-lipid complex.[7] The IR spectrum of **3** of course comprised the IR spectra of individual components.

Recently, ferrocenes are covalently linked to oligonucleotide to form electrochemical active probes[8] or monolayer films.[3b] In our system, the redox-active (outer) and hydrophobic (inner) spheres are considered to be doubly arranged around the double helix core.

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4. The standard electrochemical instrumentation consisted of a Hokuto Denko Potentiostat / Galvanostat HA-301S and a Hokuto Denko Function Generator HB-104S with a three-electrode system consisting of a glassy carbon working electrode, a platinum auxiliary electrode, and a KCl-saturated calomel reference electrode at 100 $mVs^{-1}$ scan rate.
5. The CMC value of FUT has been reported: Hoshino, K.; Saji, T. *Nippon Kagaku Kaishi* **1990**, 1014.
6. A representative procedure for preparation of a ferrocene derivative-DNA complex: To a HEPES buffer solution (5 mL, pH 8.0) of salmon sperm DNA (0.05 mmol bp) was dropwise added an aqueous solution (5 mL, HEPES buffer, pH 8.0) of FUT (0.10 mmol) at room temperature for 30 min. The obtained precipitates were gathered and freeze-dried.
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