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Dependence on the Crystallographic Orientation of Au Single Crystal Surfaces modified with Homocysteine toward Enantioselective Redox Reactions

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Effects of enantioselective interactions on redox reactions of chiral molecules were studied using Au single crystal electrodes modified with amino acids. The redox peak current densities of *R*(+)- or *S*(–)-*N, N*-dimethyl-1-ferrocenylethylamine on Au(111) modified with L- or D-homocysteine (L-/D-Hcy) depended on the combination of these chiralities. Hcy/Au(100) showed no dependence on redox peak current densities. The difference in the molecular arrangement of Hcy between Au(111) and Au(100) greatly affects enantioselective redox reactions at the electrode interface.

Keywords: Chiral molecules, Enantioselective interaction, Au single crystal electrodes

Understanding the molecular interactions between chiral molecules (enantioselective interactions) is essential for separation,[1,2] synthesis,[3,4,5] and chemical sensing.[6,7,8] Enantioselective interactions can also be applied to electrochemical sensing of redox-active, chiral molecules in solution. The enantioselective electrochemical sensing highly depends on the electrode used, which can be functionalized with self-assembled monolayers (SAMs) of chiral molecules on the surface. For such electrodes, the sensitivity can, in principle, depend not only on the type but also on the molecular arrangements of chiral molecules on the surface.

Single crystal electrodes have well-defined surfaces at the atomic level and can be modified with SAMs of chiral molecules, which is an ideal platform to understand redox reactions and the effect of the molecular arrangement at the surface on the enantioselective electrochemical sensing on the molecular scales.[9,10,11] Chiral amino acids such as cysteine, methionine, and homocysteine (Hcy) have been studied to form two-dimensional molecular ordered structures on the Au(111) surface, which originate from the dimer structure formation through hydrogen bonding.[12,13,14] On Hcy-modified Au(111) oriented substrate electrodes, redox reactions of catechin in solution are promoted or suppressed depending on the chirality combination between catechin and Hcy.[15] On single crystal surfaces with controlled atomic arrangement, redox reactions dependent on the chirality combinations have not been investigated. On the cysteine-modified Au(100) surface, cysteine forms a distinctive stripe structure, which differs from that on the Au(111) surface.[16] Such a key difference in the adsorption structure of amino acids due to the surface atomic arrangement motivates us to study the enantioselective response of chiral redox molecules in solution using Au(111) and Au(100) electrodes modified with SAMs of amino acids.

Herein, we investigated the effect of enantioselective interactions on the redox reactions between chiral, redox-active molecules and Hcy-modified Au(111) and Au(100) single crystal electrodes (**Figure 1**). As the redox molecules, *R*(+)- or *S*(–)-*N*',*N*-dimethyl-1-ferrocenylethylamine (denoted as chiral Fc or *R*(+)-/*S*(–)-Fc depending on the chirality in the following text) was used to examine the impact of Au atomic arrangements on enantioselective redox reactions.

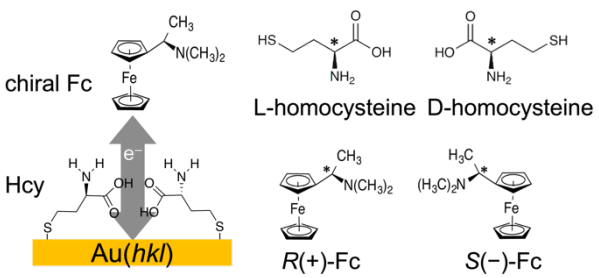


Figure 1. Schematic representation of reaction systems of chiral Fc on a Hcy-modified Au(111) or Au(100) single crystal electrode.

Au(111) and Au(100) single crystal electrodes were prepared by the flame melting method, the so-called Clavilier's method, cut in the direction of the (111) and (100) facets, subsequently polished, and then annealed at 950°C for 10 h. (see the experimental section in the Supporting Information).[17] After flame-annealing and quenching, Au single crystal electrodes were coated with SAMs of D-, L-, and DL-Hcy, which is a racemic mixture of D- and L-Hcy.

Cyclic voltammograms (CVs) of Hcy/Au(111) single crystal electrodes were recorded in an acetonitrile solution of 1 mM *R*(+)- or *S*(–)-Fc containing 0.1 M $TBAPF_6$ (**Figure 2**). All CVs show anodic and cathodic peaks at –0.04 V and –0.11 V vs. $Fc^+|Fc$, corresponding to the oxidation of the Fc moiety of chiral Fc and the reduction of the Fc^+ moiety, respectively.

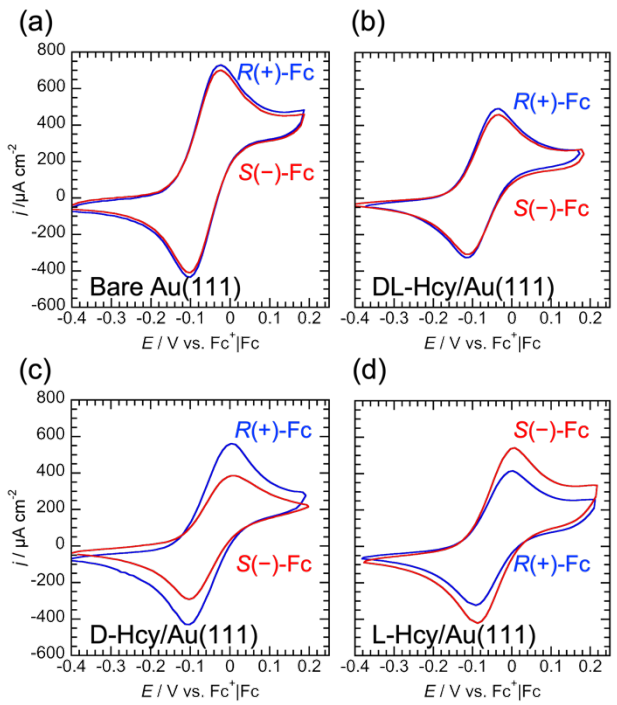


Figure 2. CVs of (a) bare Au(111) electrode, (b) DL-Hcy-, (c) D-Hcy-, and (d) L-Hcy-modified Au(111) electrodes in acetonitrile containing 0.1 M $TBAPF_6$ and 1 mM *R*(+)-Fc (the traces in blue) or *S*(–)-Fc (the traces in red). All CVs were recorded at a sweep rate of 100 mV s^{-1} under Ar.

Note that bare Au(111) electrodes showed the highest current density in the electrodes used in this work but no dependence of the peak current density on the chirality of chiral Fc (**Figure 2a**). Racemic DL-Hcy/Au(111) electrodes showed almost no dependence of the peak current densities on the chirality of chiral Fc (**Figure 2b**). The peak current densities of DL-Hcy/Au(111) are placed in the middle between those of D-Hcy/Au(111) and L-Hcy/Au(111). Peak current densities of the D- or L-Hcy/Au(111) electrodes in CVs depend on the chirality combination between chiral Fc and Hcy. The peak current density of *R*(+)-Fc at D-Hcy/Au(111) was 1.5 times higher than that of *S*(−)-Fc. (**Figure 2c**). In contrast, the opposite trend was observed at L-Hcy/Au(111) (**Figure 2d**). Compared with bare Au(111) and Hcy/Au(111) electrode, this result also support enantioselective interactions[10,18,19] between Hcy/Au(111) and chiral Fc. Thus, Hcy/Au(111) electrodes show enantioselectivity to the redox reaction of chiral Fc. Similar enantioselective effects were also reported for catechin[10] and oligopeptide.[18,19] The potential sweep rate dependence of anode current density shows a linear relationship between the peak current density and the square root of the sweep rate, indicating that the redox reaction of *R*(+)- or *S*(–)-Fc is diffusion-controlled at bare Au(111), D-, L-, or DL-Hcy/Au(111) electrodes **(Figure S1)**.

Hcy/Au(100) single crystal electrodes were used to evaluate the influence of the atomic arrangement of the Au surface on the redox response of the chiral Fc. Hcy/Au(100) showed no effect of chirality of Hcy on the peak current density for both *R*(+)and *S*(–)-Fc, although the highest peak current density was observed at bare Au(100) electrode (**Figure S2**). Thus, the difference in the Au atomic arrangement between Au(111) and Au(100) greatly impacted on the enantioselective redox reactions at the electrode interface.

To understand the difference between the adsorbed molecular arrangements of Hcy on Au(111) and Au(100), electrochemical scanning tunneling microscope (EC-STM) images of the D-Hcy/Au(*hkl*) facet were performed in 0.1 M $KClO_4$ (**Figure 3**). Small ordered domains with etching pits were formed on the Au(111) terrace (**Figure 3a**). Molecular rows aligned in the <112> ($\sqrt{3}$) directions (the angles were 30° with respect to the Au lattice directions), which is similar to the reported adlayer structure of Hcy for DL-Hcy/Au(111)[12] and L-Hcy/Au(111) (**Figure S3**).[20] In case of D-Hcy/Au(100), the adsorption of D-Hcy molecules formed characteristic stripes **(Figure 3b)**. The stripes almost aligned in the <110> direction without any etching pits. The distinctive "stripe-like" formation by Hcy adsorption is similar to that of cysteine-modified Au(100).[16] Based on the STM images, the adlayer structure of Hcy on the Au(111) surface is definitely different from that of Au(100). Two-dimensional network structures of Hcy on Au(111), which are flat in the molecular scale, can interact with chiral Fc at multiple contacts, whereas one-dimensional stripes of Hcy with Au single-atom heights on Au(100) are unlikely to interact sufficiently.

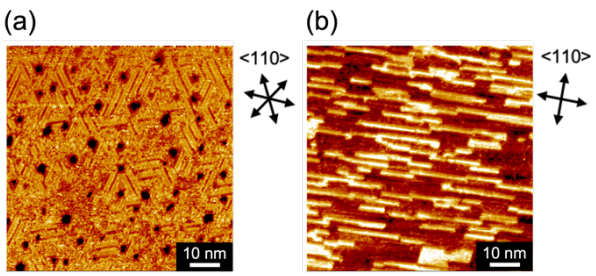


Figure 3. Typical STM images for D-Hcy on the (a) Au(111) at 0 V and (b) Au(100) surface at -0.07 V vs. Ag|AgCl (sat. KCl) in 0.1 M $KClO_4$, respectively. The tip potential was (a) -0.35 V and (b) -0.33 V vs. Ag|AgCl (sat. KCl). The tunneling current was (a) 1.25 nA and (b) 2.50 nA, respectively. A set of three or two arrows indicates the atomic direction of the Au lattice.

To assess the possibility of enantioselective adsorption of chiral Fc on the Hcy/Au(111) surface, CV measurements of the Hcy/Au(111) electrodes in electrolyte solutions without chiral Fc were performed before and after the CV measurements in solutions containing chiral Fc, as shown in **Figure 4a**. The CV of each Hcy/Au(111) electrode in the solution without chiral Fc (solid lines in **Figure 4b-e**) shows the anodic and cathodic peaks, corresponding to those observed in the solution containing chiral Fc (**Figure 2c-d**). The D-Hcy/Au(111) and L-Hcy/Au(111) tend to show higher redox peak current densities after the transfer from the

solutions with *R*(+)- and *S*(–)-Fc, respectively (**Figure 4b** and **4e**) than those used with the other chiral Fc (**Figure 4d** and **4c**). This trend is in good agreement with those observed for the CVs of Hcy/Au(111) in the presence of chiral Fc in solution (**Figure 2**). Hence, the charge density of the adsorbed chiral Fc may differ depending on the chirality combination between D- or L-Hcy and *R*(+)- or *S*(–)-Fc at Au(111). The difference in the amount of adsorbed chiral Fc depending on the combination of chirality changes the surface area of the redox-active sites on the surface, causing the peak current density to increase or decrease. The adsorbed species of chiral Fc at the Hcy/Au(111) surface are considered to mediate the diffusion-controlled electron transfer to chiral Fc. Thus, the electrochemical enantioselectivity between Hcy/Au(111) and chiral Fc originates from the adsorption of *R*(+)- or *S*(–)-chiral Fc on the electrode, which is differentiated by the adsorption structure of Hcy on Au(111).

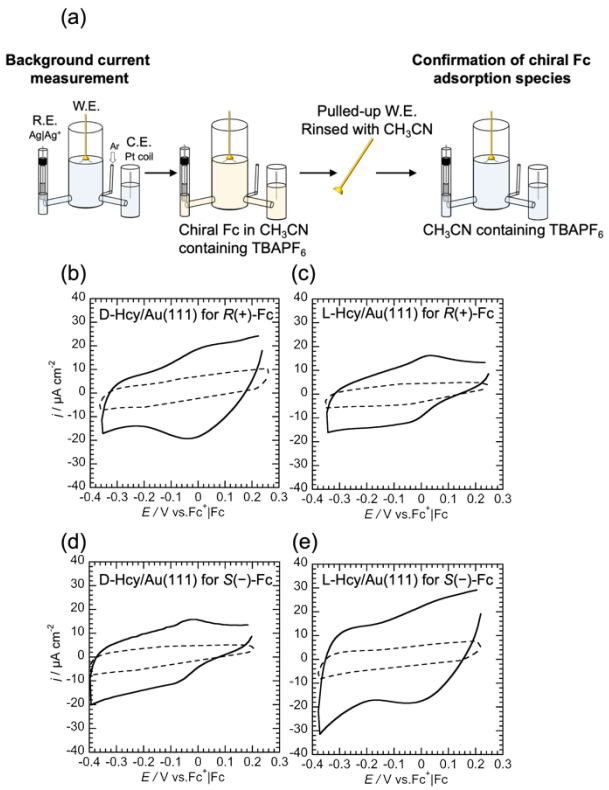


Figure 4. (a) Experimental scheme to confirm adsorption of chiral Fc: The background CVs of the Hcy/Au(111) electrodes were recorded in the electrolyte solution without chiral Fc (in b–e, the broken lines). After the CVmeasurements of Hcy/Au(111) in the electrolyte solution containing chiral Fc, the electrode was rinsed with CH_3CN to remove the excess chiral Fc, and then CVs of the same Hcy/Au electrodes were recorded again in the electrolyte solution without chiral Fc (in b–e, the solid lines). CVs of (b) D-Hcy/Au(111) and (c) L-Hcy/Au(111) electrodes transferred from the solution containing *R*(+)-Fc, and CVs of (d) D-Hcy/Au(111) and (e) L-Hcy/Au(111) electrodes transferred from the solution containing *S*(−)-Fc are shown. All CVs were recorded at a sweep rate of 100 mV s^{-1} under Ar.

In conclusions, the impact of the atomic arrangement of Au as well as the chirality combination of Hcy and Fc on the enantioselective redox reactions was investigated. The current densities of D-Hcy/Au(111) with *R*(+)-Fc and L-Hcy/Au(111) with *S*(–)-Fc were about 1.5 times higher than those of D-Hcy/Au(111) with *S*(–)-Fc and L-Hcy/Au(111) with *R*(+)-Fc. Because no dependence of redox peak current densities of Hcy/Au(100) on the chirality combination between Hcy and chiral Fc, enantioselective redox reactions are affected by the adsorption structure of Hcy, which is sensitive to the molecular arrangement of Hcy on the surface. The significant increase in redox current densities using our electrodes with controlled atomic arrangements would enable us to use various redox-active chiral molecules for fundamental studies but also open possibilities of electrochemical sensing.

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Abbreviations

R(+) or *S*(–)-Fc, *R*(+) or *S*(–)-*N*, *N*-dimethyl-1-ferrocenylethylamine; Hcy, homocysteine; SAM, self-assembled monolayer

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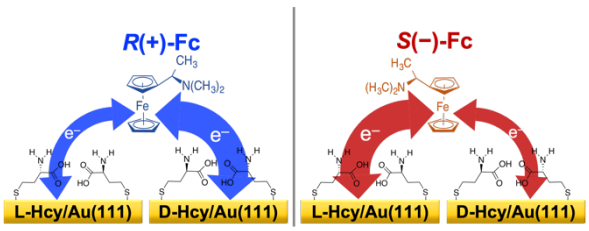
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