Enantioselectivity of Redox Reaction of DOPA at the Gold Electrode Modified with a Self-Assembled Monolayer of Homocysteine

Takuya Nakanishi,*,† Mariko Matsunaga,‡ Makoto Nagasaka,‡ Toru Asahi,†,‡ and Tetsuya Osaka*,†,‡

Institute for Biomedical Engineering, Waseda University, 513 Wasedatsurumakicho, Shinjuku, Tokyo 162-0041, Japan, and School of Science and Engineering, Waseda University, 3-4-1 Okubo, Shinjuku, Tokyo 169-8555, Japan

Received April 7, 2006; E-mail: takn@waseda.jp; osakatet@waseda.jp

Enantioselective reduction and oxidation reactions at solid surfaces are important for enantioselective heterogeneous catalysts[1] and relevant electrodes.[2,3] An electrochemical approach provides fundamental information on those enantioselective reactions, and it also enables discriminative sensing of enantiomers.[4–10] Because imparting chirality to a solid surface by modification with chiral components is a feasible approach for the discrimination, the enantioselectivity of electrochemical reactions has been investigated by using electrodes modified with ultrathin chiral films, often with the aim of application to chiral sensing.[6–10] With the recent progress in electrochemical surface science,[11] well-ordered surfaces, such as single-crystal electrodes and electrodes modified with a self-assembled monolayer (SAM), have become useful for investigating electrode reactions at an atomic or molecular level. For chiral electrode reactions, electrodes with an ordered atomic or molecular arrangement with chirality are expected to exhibit enantioselectivity, as reported for metal (Pt and Au)[12] and oxide (CuO)[13] surfaces with a chiral crystallographic orientation. As for achiral single-crystal surfaces, the modification with chiral molecules was reported to bring about an ordered molecular arrangement with two-dimensional chirality,[14,15] for which enantioselectivity is expected to appear not simply from a one-to-one interaction between the modifier and the analyte molecules but from nanosized spaces formed by the molecular arrangement of modifier on the surface. Indeed, we already demonstrated a unique enantioselectivity of the SAM-modified gold surface with chiral molecular arrangement.[16]

In this study, we focused our attention on the enantioselectivity of the SAM of homocysteine (Hcy), $HSCH_2CH_2CH(NH_2)COOH$, formed on the (111)-oriented gold surface, and the redox behavior of 3,4-dihydroxyphenylalanine (DOPA), which is an electrochemically active chiral molecule, was analyzed by cyclic voltammetry at a gold electrode modified with one of the two enantiomeric forms of Hcy. Although several studies on polycrystalline gold electrodes modified with Hcy have been performed,[17] the work reported here represents the first investigation on the enantioselectivity of the Hcy-modified gold electrode.

A gold film (200 nm in thickness) with predominantly (111)-oriented surfaces was prepared by vapor deposition on a quartz substrate with a 15-nm-thick titanium metal as an adhesive layer. After flame annealing, the substrate was immersed into a 0.5 mM ethanolic solution of homocystine, the dimer of Hcy, for 24 h to prepare the SAM. Electrochemical measurements were carried out in aqueous solutions containing 0.25 M H_2SO_4 or K_2SO_4 as the supporting electrolyte. The solutions were deoxygenated with purified argon for at least 30 min prior to the measurements. A $Hg/Hg_2SO_4/K_2SO_4$ (0.5 M, aqueous) electrode and a platinum wire were used as the reference and the counter electrode, respectively.

---

† Institute for Biomedical Engineering.
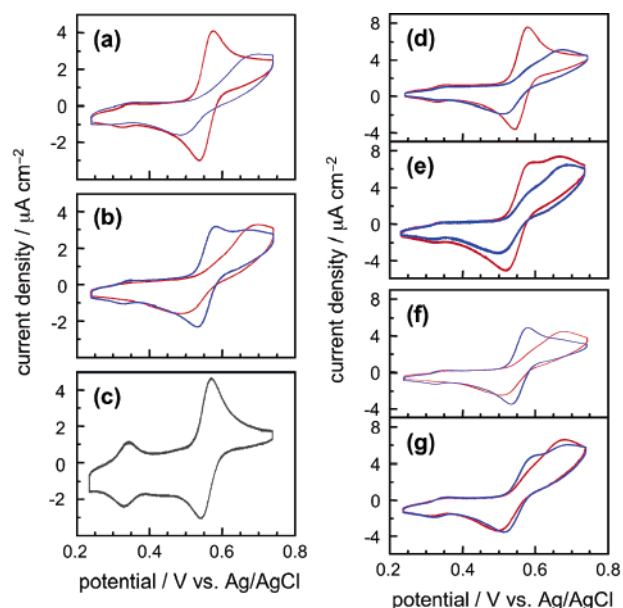‡ School of Science and Engineering.

Figure 1. Cyclic voltammograms for redox reactions of DOPA at gold electrodes modified with (a, d, e) L- and (b, f, g) D-Hcy in aqueous 0.25 M H_2SO_4. Red and blue curves represent the voltammograms for D- and L-DOPA, respectively. (c) Obtained with bare gold electrode for L-DOPA. Concentrations of DOPA were (a–c) 40, (d, f) 60, and (e, g) 100 μM. Scan rate was 5 mV s^{-1}.

All potentials reported in this paper are referred to the Ag/AgCl/KCl (saturated, aqueous) electrode.

Figure 1a,b shows cyclic voltammograms for the redox reactions of 40 μM D- and L-DOPA at the gold electrode modified with L- and D-Hcy in 0.25 M H_2SO_4. The shape of the voltammogram was found to depend on the combination of the chirality of Hcy and that of DOPA. For the electrode modified with L-Hcy (Figure 1a), coupled anodic (oxidation) and cathodic (reduction) peaks were observed at 0.58 and 0.53 V (vs Ag/AgCl), respectively, for D-DOPA, while broad anodic and cathodic waves were observed at 0.68 and 0.48 V, respectively, for L-DOPA. With the electrode modified with D-Hcy (Figure 1b), on the other hand, the voltammogram for L-DOPA exhibited a pair of redox peaks at 0.58 and 0.53 V, whereas broad waves at 0.68 and 0.48 V were observed for D-DOPA. In comparison with the voltammogram obtained with a bare gold electrode (Figure 1c), in which the anodic and cathodic peaks due to the 2-electron-2-proton oxidation and reduction of the DOPA/dopaquinone couple appeared at 0.58 and 0.55 V, respectively,[18] the Hcy monolayer of one enantiomeric form was suggested to block the redox reaction of only one enantiomer of DOPA, with cross inversion for the other enantiomer.

The amount of Hcy molecules self-assembled on gold was estimated from the electric charge for the reductive desorption of the SAM in 0.5 M KOH,[19] and it was found to be approximately
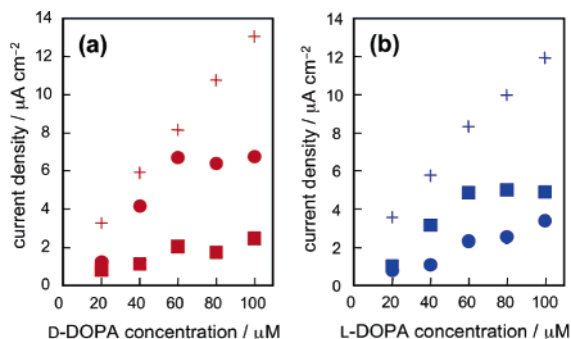
Figure 2. Concentration dependence of the anodic current density for the peak or the shoulder observed at 0.58 V in 0.25 M H_2SO_4 containing (a) D- and (b) L-DOPA. Circles and squares indicate current density values measured at gold electrodes modified with L- and D-Hcy, respectively. Crosses show current density values measured at bare gold electrode.

1.8×10^{14} molecules cm^{-2}.[20] This value is close to the number of molecules expected from the $(2\sqrt{3} \times 3\sqrt{3})R30°$ structure reported for the adlayer of DL-Hcy on the gold(111) surface in 0.1 M $HClO_4$,[21] which corresponds to a fractional coverage of one-ninth of the number density of surface gold atoms. If it is assumed that the nanosized open spaces or apertures between Hcy molecules in the SAM, through which bare gold atoms are exposed, allow further access of small molecules to the gold surface,[22] the enantioselective blocking of the redox reaction of DOPA can be attributed to the steric hindrance between DOPA and the chiral space provided by arranged Hcy molecules.

In the solutions containing high concentrations of DOPA (Figure 1d−g), two anodic waves were observed at 0.58 and 0.68 V; the anodic peak at 0.68 V was clearly seen in the voltammograms for D-DOPA/L-Hcy and L-DOPA/D-Hcy pairs, while the shoulder of the anodic wave appeared at 0.58 V for L-DOPA/L-Hcy and D-DOPA/D-Hcy pairs. On the other hand, the cathodic peak was broad, as the two peaks at 0.53 and 0.48 V overlapped with each other. Figure 2 shows the dependence of anodic current density at 0.58 V on the DOPA concentration. The magnitude of anodic current density at 0.58 V for D-DOPA/L-Hcy and L-DOPA/D-Hcy pairs increased with increasing DOPA concentration, and it tended to be saturated at the concentrations higher than 60 μM, whereas the current increased linearly up to at least 100 μM at the bare gold electrode. Here, the current densities at 0.58 V for D- and L-DOPA/D-Hcy tended to be somewhat smaller than those for L- and D-DOPA/L-Hcy, respectively, probably because of the difference in the degree of structural orderliness of the SAM.[20]

The appearance of the two pairs of redox waves indicates that there are two different paths for the electron transfer between the DOPA molecule and the electrode. One involves DOPA molecules accessible to the gold surface as described above, which gives rise to the pair of redox peaks with a peak-to-peak separation of 50 mV. This magnitude of peak-to-peak separation is greater by 20 mV than the 30 mV separation observed for the bare gold electrode. The saturation of anodic current in Figure 2 is accounted for by this area-restricted electron transfer. The other is the electron transfer across the SAM associated with the pair of redox peaks separated by as much as ~200 mV, indicating retarded electron transfer.[23]

Notably, the enantioselective blocking of the redox reaction of DOPA was not observed in the buffered 0.25 M K_2SO_4 solution at pH 5.5, which is higher than the pK_a of the carboxyl group in both Hcy and DOPA. As the intermolecular hydrogen bond between carboxyl groups is responsible for the formation of the ordered adlayer structure of Hcy in the acidic condition,[21] the orientation and conformation of Hcy molecules self-assembled on gold are considered to depend on pH, providing the different environment for nanosized spaces.[24]

In summary, the Hcy-modified gold electrode with (111)-oriented surface was shown to exhibit enantioselectivity in the redox reaction of DOPA in acidic solution. The result indicates the importance of nanosized chiral spaces as the enantioselective site.

Supporting Information Available: Additional voltammograms. This material is available free of charge via the Internet at http://pubs.acs.org.

References

(1) Blaser, H.-U. *Tetrahedron: Asymmetry* **1991**, *2*, 843.
(2) Watkins, B. F.; Behling, J. R.; Kariv, E.; Miller, L. L. *J. Am. Chem. Soc.* **1975**, *97*, 3549.
(3) Komori, T.; Nonaka, T. *J. Am. Chem. Soc.* **1984**, *106*, 2656.
(4) Kataky, R.; Bates, P. S.; Parker, D. *Analyst* **1992**, *117*, 1313.
(5) Abbott, A. P.; Barker, G. W.; Davies, D. L.; Griffiths, G. A.; Walter, A. J.; Kocovsky, P. *Anal. Chem.* **2002**, *74*, 4002.
(6) Tao, G.; Katz, E.; Willner, I. *Chem. Commun.* **1997**, 2073.
(7) Fukuda, T.; Maeda, Y.; Kitano, H. *Langmuir* **1999**, *15*, 1887.
(8) Kashiwagi, Y.; Uchiyama, K.; Kurashima, F.; Anzai, J.-i.; Osa, T. *Electrochemistry* **1999**, *67*, 900.
(9) Sheridan, E. M.; Breslin, C. B. *Electroanalysis* **2005**, *17*, 532.
(10) Fireman-Shoresh, S.; Turyan, I.; Mandler, D.; Avnir, D.; Marx, S. *Langmuir* **2005**, *21*, 7842.
(11) Kolb, D. M. *Angew. Chem., Int. Ed.* **2001**, *40*, 1162.
(12) (a) Attard, G. A. *J. Phys. Chem. B* **2001**, *105*, 3158. (b) Attard, G. A.; Ahmadi, A.; Feliu, J.; Rodes, A.; Herrero, E.; Blais, S.; Jerkiewicz, G. *J. Phys. Chem. B* **1999**, *103*, 1381. (c) Martins, A.; Ferreira, V.; Queirós, A.; Aroso, I.; Silva, F.; Feliu, J. *Electrochem. Commun.* **2003**, *5*, 741.
(13) Switzer, J. A.; Kothari, H. M.; Poizot, P.; Nakanishi, S.; Bohannan, E. W. *Nature (London)* **2003**, *425*, 490.
(14) Ohtani, B.; Shintani, A.; Uosaki, K. *J. Am. Chem. Soc.* **1999**, *121*, 6515.
(15) Lorenzo, M. O.; Baddeley, C. J.; Muryn, C.; Raval, R. *Nature (London)* **2000**, *404*, 376.
(16) (a) Nakanishi, T.; Yamakawa, N.; Asahi, T.; Osaka, T.; Ohtani, B.; Uosaki, K. *J. Am. Chem. Soc.* **2002**, *124*, 740. (b) Nakanishi, T.; Yamakawa, N.; Asahi, T.; Shibata, N.; Ohtani, B.; Osaka, T. *Chirality* **2004**, *16*, S36.
(17) (a) Zhang, H.-M.; Li, N.-Q.; Zhu, Z. *Microchem. J.* **2000**, *64*, 277. (b) Zhang, H.-M.; Zhou, X.-L.; Hui, R.-T.; Li, N.-Q.; Liu, D.-P. *Talanta* **2002**, *56*, 1081.
(18) The pair of anodic and cathodic waves observed at 0.35 and 0.34 V, respectively, is attributable to the redox reaction concerning 6-hydroxy-dopa, which is formed from DOPA and water in acidic solution. See: Brun, A.; Rosset, R. *J. Electroanal. Chem.* **1974**, *49*, 287.
(19) Widrig, C. A.; Chung, C.; Porter, M. D. *J. Electroanal. Chem.* **1991**, *310*, 335.
(20) The width of the current peak corresponding to the reductive desorption of L-Hcy tended to be slightly broader than that of D-Hcy, which is attributable to a difference in the degree of orderliness of the SAM.
(21) Zhang, H.-M.; Su, G.-J.; Wang, D.; Wan, L.-J.; Jin, G.; Bai, C.-L.; Zhou, X. *Electrochim. Acta* **2004**, *49*, 1629.
(22) In the case of cyclic voltammetry for the solution containing dopamine or catechol, each of which has the same redox moiety as that of DOPA, at the L-Hcy-modified gold electrode, the shape of the voltammograms was similar to that obtained for D-DOPA, not to that for L-DOPA.
(23) Bard, A. J.; Faulkner, L. R. *Electrochemical Methods: Fundamentals and Applications;* John Wiley & Sons: New York, 1980.
(24) The enantioselectivity also disappeared with a less (111)-dominant gold film as a substrate even in acidic solution.

JA062380F