

Coupling of acid–base and redox functions in mixed sulfide monolayers on gold

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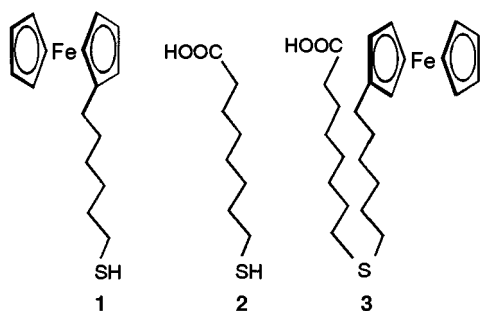
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A mixed acid-ferrocene self-assembled sulfide monolayer on gold shows a pH-dependent electrochemical response by through-space communication between the receptor and ferrocene readout unit.

Self-assembled monolayers on gold show great promise for a variety of applications.¹ Recently, we reported the electrochemical detection by electrochemical impedance spectroscopy of the selective complexation of alkali and alkaline-earth cations ($\text{Na}^+_{\text{aq}}/\text{K}^+_{\text{aq}} > 100$) by self-assembled monolayers of crown ethers.² The advantage of electrochemically-active (*e.g.* ferrocene) monolayers is that the redox signal can be used as an internal readout.^{1b} Mixed ferrocene-thiol/alkanethiol monolayers form complexes with calix[6]arene, and β - and γ -cyclodextrin from aqueous solution.³ Rojas and Kaifer reported that the interaction of catechol or indole with a mixed monolayer of thiolated paraquat and decanethiol gives a cathodic shift of the redox potential.⁴ A more general electrochemical detection of electrochemically-inactive compounds would be possible by decoupling the redox center and the receptor.⁵ Complexation by the receptor in close proximity of the redox center should change the redox properties. Here we describe such a system in which protonation and deprotonation of a carboxylate group is detected *via* a ferrocene readout unit.

This concept was first studied in a mixed monolayer of ferrocene-thiol **1** and acid-thiol **2**^{6,7} because it is known that



ferrocene monolayers are pH-independent.⁸ Mixed monolayers were prepared from a solution containing a 1:3 ratio of ferrocene-thiol **1** and acid-thiol **2**.⁹ The adsorbed monolayer has about half of the surface covered by ferrocene-thiol and the other half by acid-thiol (pure Fc-**1** monolayer: $Q = 19.5 \mu\text{C}$;¹⁰ mixed Fc-**1**/acid-**2** SAM: $Q = 8.6 \mu\text{C}$). Fig. 1 shows the redox signal for the system at pH 1 and 11.¹¹ At high pH deprotonation of the acid group introduces a negative charge in the monolayer which stabilizes the ferrocenium ion and this results in a cathodic shift of the redox signal. The pH can be switched backward and forward leading to a small (around 10%) loss in ferrocene signal over a large number of measurements at different pHs, indicating a fairly stable system. Reductive desorption of the monolayer occurs at more cathodic potentials.¹² The cyclic voltammogram at high pH shows two very broad peaks: part of the ferrocene centers is responsive to the

pH, the other part is not. Apparently, not all ferrocenes experience the same influence of deprotonation of the acid function. This is an indication of an inhomogeneous monolayer.¹³

This problem of inhomogeneity was circumvented by covalently linking the two components, which is very simply achieved in a mixed *sulfide* like **3**.¹⁴ With this molecule, domain formation is impossible and the covalent attachment forces a 1:1 ratio of the binding site and the redox center. This is one of the very few examples of a monolayer adsorbate with multiple functional units.¹⁵ We prepared monolayers of sulfide **3** that were characterized by wettability studies, X-ray photoelectron spectroscopy (XPS), time-of-flight secondary ion mass spectrometry (TOF-SIMS) and electrochemistry. Contact angles with water indicated a surface with moderate polarity and the hysteresis between the advancing and receding angle shows a disordered monolayer ($\theta_{\text{adv/rec}} [\text{H}_2\text{O}]$: 64–20). XPS measurements of the monolayer show all the elements of the adsorbate (Fe, C, O, and S) in fair correspondence with the expected relative ratios (C:S ratio/calc.:found = 32:1/31:1). In the positive scan of the TOF-SIMS measurements the peaks for M^+ (444) and $[\text{M} + \text{Au} + \text{H}]^+$ (642) give further evidence that sulfides adsorb without C–S bond breaking on gold.¹⁶ Electrochemical characterization showed all the characteristics of electrochemically-active monolayers, *e.g.* a linear dependence of the redox current on the scan rate. Calculation of the ferrocene charge ($4.5 \mu\text{C}$) indicates a loosely-packed monolayer, by comparison with the charge related to the pure ferrocene-thiol **1**, and mixed ferrocene-thiol **1**/acid-thiol **2** monolayers described above. The relatively high hysteresis found in the wettability studies and the moderate ferrocene coverage obtained from cyclic voltammetry confirm our previous finding^{11a} that sulfides that are connected by one attachment point to gold, forming loosely-packed monolayers.¹⁷

The electrochemical response of the sulfide **3** monolayer is strongly influenced by the pH of the electrolyte solution (Fig. 2). The redox signal shifts cathodically but hardly broadens. This latter phenomenon is consistent with a homogeneous monolayer. These cyclic voltammograms reveal the communication between the components of the mixed sulfide monolayer, *i.e.* the redox unit senses the protonation and

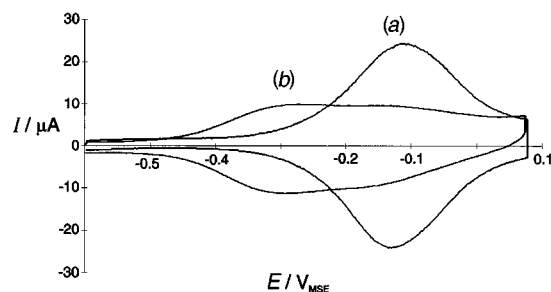


Fig. 1 Electrochemical response of a mixed ferrocene-thiol **1**/acid-thiol **2** monolayer. (a) pH 1, 0.1 M HClO_4 ; (b) pH 11, 0.1 M NaClO_4 + 1 mM NaOH [$0 \text{ V}_{\text{MSE}} = +0.61 \text{ V}_{\text{NHE}}$].

deprotonation of the carboxylate group. Titration with mixtures of different pH (HClO_4 , NaClO_4 , and NaOH) shows a strong dependence of the redox potential on the pH (Fig. 3).¹⁸ With increasing pH values the carboxylates stabilize the ferrocenium state of the redox couple, and as a consequence the redox potential shifts cathodically. The ferrocene response curve shifts over a large pH window. It is known that the $\text{p}K_a$ value for organic acids which in solution is about 3–4, increases for well-packed monolayers to 6–7.¹⁹ The loose packing of monolayers of sulfides using one attachment point can result in a more exposed acid function, which will have a lower $\text{p}K_a$, more comparable to the solution value of 3–4. Furthermore, it is important to note that Fig. 3 is not the titration curve of the acid function in the monolayer, but the response of a complex multicomponent system to changes in the pH of the electrolyte solution. The electrochemical oxidation of ferrocene to ferrocenium might change the *apparent* $\text{p}K_a$ of the acid function, rendering the communication mutual. A similar effect was recently described by Corn *et al.*, who showed by SPR measurements that the adsorption of the positively charged avidin on an acid-terminated monolayer shifted the apparent $\text{p}K_a$ to lower values.²⁰

A self-assembled monolayer consisting of receptor and readout units can be used to detect electrochemically-inactive compounds electrochemically. Here we have shown the pH-dependent response of mixed acid-ferrocene monolayers. At the moment we are investigating the effect on the redox signal of the ferrocene unit of the binding to the carboxylate groups of different cations. Preliminary results indicate that the binding properties of $\text{Et}_4\text{N}^+_{\text{aq}}$, and Na^+_{aq} or K^+_{aq} to the carboxylate groups (low and high binding, respectively) are reflected in the cyclic voltammograms.

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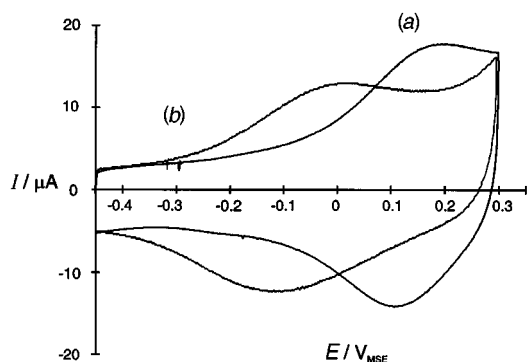


Fig. 2 Electrochemical response of a ferrocene-acid-sulfide **3** monolayer: (a) pH 1, 0.1 M HClO_4 , (b) pH 6.5, 0.1 M NaClO_4 [$0 \text{ V}_{\text{MSE}} = +0.61 \text{ V}_{\text{NHE}}$].

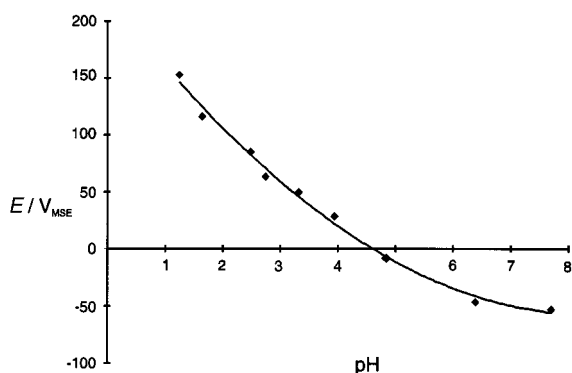


Fig. 3 Dependence of the formal potential of the ferrocene unit in a monolayer of sulfide **3** on the pH of the electrolyte solution [$0 \text{ V}_{\text{MSE}} = +0.61 \text{ V}_{\text{NHE}}$].

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