

Templated SAMs for metal ion recognition

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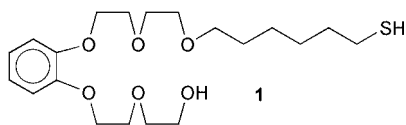
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Self assembled monolayers of a polyether derivative selectively detect potassium cations when templated in their presence.

Self-assembled monolayers (SAMs) that incorporate receptor molecules can act as molecular recognition interfaces and thus as selective sensors for specific analytes.^{1–3} Binding sites can also be formed within the SAMs during their preparation, if they are grown in the presence of appropriate analytes that template the aggregation processes.⁴ This process could also be described as molecular imprinting, although this term is usually reserved for polymer systems, where binding of functionalized monomers by a template molecule is followed by polymerization and template removal.^{4–6} Well-defined cavities with selective binding properties are thus formed in the polymeric backbone which are able to recognize analytes that are similar or identical to the template.

The first preliminary report involving imprinted SAMs was published by Sagiv⁷ in 1979, but the concept went largely unexplored for a long time until recently, when the strategy was employed to generate binding sites for organic substrates at the surface of modified electrodes.^{8–11} It seems as if more examples are appearing more frequently, probably due to the simplicity of the approach which largely relies on the principle of self-assembly and requires minimal synthetic effort. Perhaps surprisingly and to the best of our knowledge, no examples of SAM formation involving metal ions as templates have been reported to date. In this communication, we report the preparation and the electrochemical investigation of potassium-templated SAMs on gold which selectively detect K⁺ but not Na⁺.

Receptor **1** was designed to bind metal cations in the polyether loop, which was purposely fused to the aromatic ring



for rigidity, but allowed to retain enough flexibility for intra- as well as inter-molecular templating upon self-assembly on the gold surface. The thiol group provides the anchoring point to the gold substrate. The polymethylene spacer separating the polyether recognition site and the anchoring group should facilitate the formation of the monolayers by van der Waals forces. The compound was synthesized in three steps. Reaction of catechol with 2-chloroethoxyethanol afforded a diol **2**, which was monoalkylated with a small excess of 1,6-dibromohexane. Finally, the resulting bromide **3** was converted into **1** by treatment with thiourea followed by basic hydrolysis.[†]

SAMs **A** and **B** were prepared by immersing glass-sealed gold bead electrodes for 24 h in an EtOH solution of **1** (1 mM) (**A**) or an EtOH–H₂O (1 : 1) solution of **1** (1 mM) and KCl (0.1 M) (**B**). The electrodes were then rinsed with H₂O, EtOH and CH₂Cl₂ and dried under a stream of Ar. Impedance measurements were performed using an aqueous solution of Et₄NCl (0.1 M) and [Ru(NH₃)₆]Cl₃ (1 mM), a SAM modified gold bead as the working electrode, a coiled platinum counter electrode and

a Ag/AgCl reference electrode. Experiments were conducted at the formal redox potential of the [Ru(NH₃)₆]^{3+/2+} couple with a frequency ranging from 100 kHz to 0.1 Hz. The spectra were analyzed by the 'EquivalentCircuit'¹² software package. Binding of cations to the receptor moiety of a non-electroactive SAM can be monitored by impedance spectroscopy using the positively charged redox couple [Ru(NH₃)₆]^{3+/2+} as a probe.¹³ An increase in the charge transfer resistance (*R*_{ct}) is observed upon complexation of the metal cations,^{13,17} and is due to electrostatic repulsion between the cation and the positively charged ruthenium redox couple. These changes were used to monitor the recognition of alkali metal cations by monolayers of **1**.

The charge transfer resistances (*R*_{ct}) of the SAMs **A** and **B** were measured in the presence of increasing concentrations of KCl. For **A** [Fig. 1(a)], *R*_{ct} is 1.35 kΩ cm² immediately after preparing the SAM and in the absence of KCl. Upon KCl additions, *R*_{ct} increases slightly until it reaches a limiting value of 2.14 kΩ cm² at a salt concentration of 100 mM. Thus, the effect of salt addition is reasonably small. For **B** [Fig. 1(b)], *R*_{ct} is 2.20 kΩ cm² in the absence of KCl but upon addition of this salt the resistance increases dramatically and reaches a value of

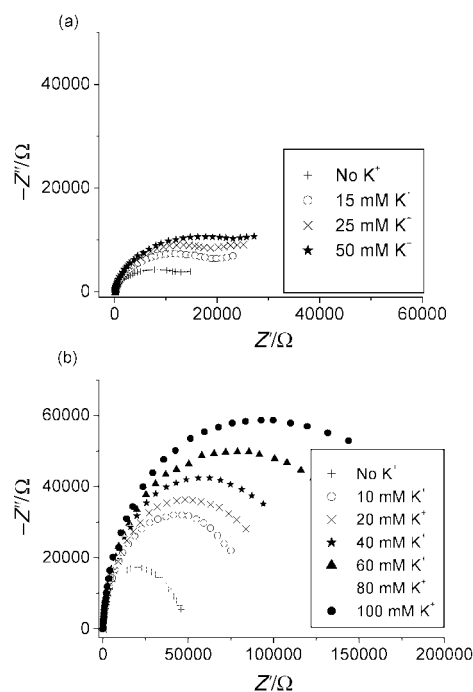


Fig. 1 (a) Nyquist electrochemical impedance spectroscopy plot of the monolayer of **1** grown in the absence of KCl (**A**), and exposed to different K⁺ concentrations. Experiments were conducted in H₂O, using Et₄NCl (0.1 M) as supporting electrolyte and [Ru(NH₃)₆]Cl₃ (1 mM) as redox probe at *E* = −0.165 V and the frequency range 100 kHz–0.1 Hz. (b) Nyquist electrochemical impedance spectroscopy plot of the monolayer of **1** grown in the presence of 0.1 M KCl (**B**), and exposed to different K⁺ concentrations. Experiments were conducted in H₂O, using Et₄NCl (0.1 M) as supporting electrolyte and [Ru(NH₃)₆]Cl₃ (1 mM) as redox probe at *E* = −0.165 V in the frequency range 100 kHz–0.1 Hz.

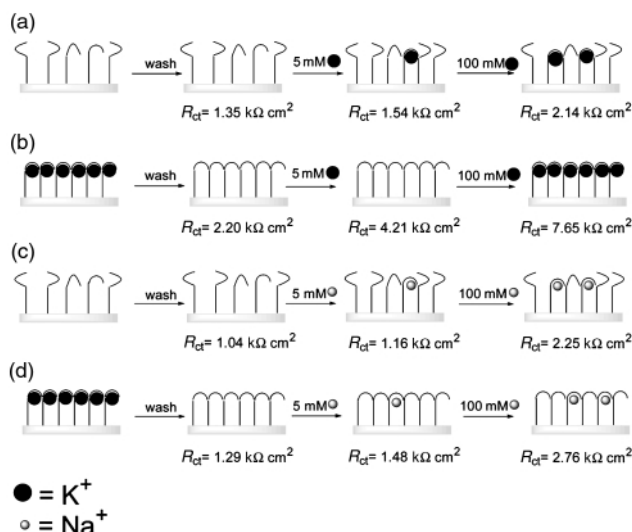


Fig. 2 Cartoon representation of the binding of metal cations by SAM of **1** grown: (a) in the absence of KCl (**A**), K^+ titration; (b) in the presence of 0.1 M KCl (**B**), K^+ titration; (c) in the absence of KCl (**A**), Na^+ titration; (d) in the presence of 0.1 M KCl (**B**), Na^+ titration.

7.65 $k\Omega\text{ cm}^2$ at a salt concentration of 100 mM. The area coverage for monolayers **A** ($\phi_A = 1.96 \times 10^{-9}\text{ mol cm}^{-2}$) and **B** ($\phi_B = 2.43 \times 10^{-9}\text{ mol cm}^{-2}$) were determined by reductive desorption in a 0.5 M KOH solution,¹⁸ and are in accordance with the relative R_{ct} values of **A** and **B**. The association constants (K) for potassium binding by **A** and **B** were determined by fitting the experimental R_{ct} values and concentrations of KCl using a Langmuir isotherm.¹³ The value of K was found to be $124 \pm 20\text{ M}^{-1}$ for **A** and $353 \pm 30\text{ M}^{-1}$ for **B**. The difference between these two values demonstrates that the templated monolayer **B** has a higher binding affinity for potassium cations than **A**. In the case of **B**, the self-assembly of **1** on gold is assisted by the cations which induce the formation of optimal binding domains [Fig. 2(b)]. The resulting pre-organized recognition sites favor cation recognition at the interface. The template effect is also reflected in the response to changes in cation concentration. The addition of 5 mM KCl produces a small change in the R_{ct} of **A** but a large increase in the R_{ct} of **B** [Fig. 2(a) and (b)].

The ability of **A** and **B** to recognize sodium cations was also tested. In both instances, however, small changes in the R_{ct} values were observed [Fig. 2(c) and (d)] upon addition of NaCl, suggesting that recognition of Na^+ ions by the monolayer of **1** is very modest. Interestingly, the R_{ct} of the templated monolayer **B** is only 2.76 $k\Omega\text{ cm}^2$ in the presence of 100 mM NaCl. This monolayer has instead a R_{ct} of 7.65 $k\Omega\text{ cm}^2$ in the presence of 100 mM KCl. The different behavior indicates that **B** has a pronounced selectivity for potassium cations.

Summarizing, we have demonstrated for the first time that binding sites for potassium cations can be imprinted into SAMs when the monolayer is assembled on gold in the presence of this metal cation. The resulting modified gold electrodes detect potassium cations in water with good selectivity over sodium cations. This approach to chemical sensors is simple and efficient and can be easily extended to the realization of SAMs for the recognition of analytes other than potassium cations.

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Notes and references

† *Experimental conditions*: Preparation of 2-(2-[2-(2-hydroxyethoxy)ethoxy]phenoxy)ethoxyethanol **2**: a mixture of catechol (5.5 g, 50 mmol) and K_2CO_3 (35 g, 250 mmol) in anhydrous MeCN, was heated for 30 min under a stream of Ar. 2-Chloroethoxyethanol (14.9 g, 120 mmol) was added and reflux was maintained for 40 h. The suspension was then filtered and the solids washed with CH_2Cl_2 (150 mL). The combined organic phases were evaporated under reduced pressure and the residue was re-dissolved in CH_2Cl_2 (150 mL) and washed with water ($3 \times 50\text{ mL}$). Purification by column chromatography [SiO_2 , CH_2Cl_2 -EtOAc (1:1)] to EtOAc-EtOH (9:1) afforded **2** in 44% yield.

Preparation of 2-[2-(2-[2-(6-bromohexyloxy)ethoxy]ethoxy)phenoxy]ethoxyethanol **3**: a mixture of **2** (0.9 g, 3.15 mmol) and NaH (60% in mineral oil) (0.36 g, 9 mmol) in anhydrous THF (200 mL) was stirred at room temperature under a stream of Ar. After 30 min 1,6-dibromohexane (4.76 g, 19.5 mmol) was added and the mixture was left stirring for 16 h. After addition of MeOH the solvent was evaporated under reduced pressure. The residue was dissolved in CH_2Cl_2 (200 mL) and washed with H_2O ($3 \times 100\text{ mL}$). Purification by column chromatography [SiO_2 , hexane-EtOAc (1:1)] afforded **3** in 76% yield.

Preparation of 2-[2-(2-[2-(6-mercaptohexyloxy)ethoxy]ethoxy)phenoxy]ethoxyethanol **1**: a solution of **2** (1.2 g, 2.7 mmol) and thiourea (0.813 g, 10.7 mmol) in EtOH (80 mL) was left refluxing under a stream of Ar for 16 h. The solvent was evaporated under reduced pressure and the residue suspended in an aqueous solution of KOH (60 mL, 0.84 g, 15 mmol), and stirred for 2 h. The reaction mixture was acidified with HCl and CH_2Cl_2 (150 mL) was added. Washing with H_2O ($3 \times 100\text{ mL}$) and purification by column chromatography afforded **1** in 33% yield. $\delta_H(CDCl_3)$ 1.28–1.39 (5H, m), 1.54–1.63 (4H, m), 2.48 (2H, t, J 7.3 Hz), 3.45 (2H, t, J 6.7 Hz), 3.59 (2H, t, J 5.2 Hz), 3.64–3.76 (6H, m), 4.12–4.20 (4H, m), 6.88–6.90 (4H, m); m/z (FAB+): 402 (M^+ , 70%), 403 ($M^+ + 1$, 100%).

- S. Flink, F. C. J. M van Veggel and D. N. Reinhoudt, *Adv. Mater.*, 2000, **12**, 1315.
- R. M. Crooks and A. J. Ricco, *Acc. Chem. Res.*, 1998, **31**, 219.
- A. E. Kaifer, *Isr. J. Chem.*, 1996, **36**, 389.
- K. Haupt and K. Mosbach, *Chem. Rev.*, 2000, **100**, 2495.
- H. Asanuma, T. Hishiya and M. Komiyama, *Adv. Mater.*, 2000, **12**, 1019.
- G. Wulff, *Angew. Chem., Int. Ed. Engl.*, 1995, **34**, 1812.
- J. Sagiv, *Isr. J. Chem.*, 1979, **18**, 346.
- V. M. Mirsky, T. Hirsch, S. Piletsky and O. S. Wolfbeis, *Angew. Chem., Int. Ed.*, 1999, **38**, 1108.
- M. Lahav, E. Katz, A. Doron, F. Patolsky and I. Willner, *J. Am. Chem. Soc.*, 1999, **121**, 862.
- O. Chailapakul, R. M. Crooks, C. B. Ross, L. Sun and J. Schorer, *Interfacial Design and Chemical Sensing*, ed. T. E. Mallouk and D. J. Harrison, ACS Symp. ser. 561, Washington, DC, 1994.
- S. A. Piletsky, E. V. Piletskaya, T. A. Sergeeva, T. L. Panasyuk and A. V. El'skaya, *Sens. Actuators B*, 1999, **60**, 216.
- B. A. Boukamp, Equivalent Circuit version 4.55, University of Twente, Department of Chemical Technology, Enschede, The Netherlands, 1996.
- S. Flink, B. A. Boukamp, A. van der Berg, F. G. J. M. van Veggel and D. N. Reinhoudt, *J. Am. Chem. Soc.*, 1998, **120**, 4652.
- S. Flink, F. G. J. M. van Veggel and D. N. Reinhoudt, *J. Phys. Chem. B*, 1999, **103**, 6515.
- K. Bandyopadhyay, H. Liu, S.-G. Liu and L. Echegoyen, *Chem. Commun.*, 2000, 141.
- K. Bandyopadhyay, H. Liu, S.-G. Liu and L. Echegoyen, *Chem. Eur. J.*, 2000, **6**, 1176.
- K. Bandyopadhyay, H. Liu, S.-G. Liu and L. Echegoyen, *Langmuir*, 2000, **16**, 2706.
- Y. Wang and A. E. Kaifer, *J. Phys. Chem. B*, 1998, **102**, 9922.