Effects of anionic sites on the selectivity of sodium-sensitive CHEMFETs

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Abstract

Calix[4]arene amides incorporated in poly(vinyl chloride) membranes provide good Na⁺ selectivity for CHEMFETs. A remarkable difference in the Na⁺/Ca²⁺ selectivity was observed depending on the presence or absence of tetraphenylborate ions in the membrane matrix. In the latter case the potentiometric selectivity coefficient ($\log K_{\text{Na,Ca}}^{\text{Pot}}$) increased from -2.1 to -3.6 . Calix[4]arene amides proved to be excellent ionophores to obtain Na⁺ selectivity in the presence of K⁺, i.e. $\log K_{\text{Na,K}}^{\text{Pot}} = -2.7$.

Introduction

Since the construction of a potassium-sensitive field-effect transistor (FET) by Moss *et al.* [1], chemically modified FETs for selective ion detection have become of increasing interest. Moss *et al.* introduced the potassium sensitivity by the natural K⁺-selective ionophore valinomycin, in a plasticized poly(vinyl chloride) (PVC) membrane which was physically attached to the gate surface of the FET. However, the sensitivity for other cations or anions is mainly introduced by synthetic ionophores. In general, ionophores, whether natural or synthetic, are characterized by a cavity of molecule-sized dimensions that enables selective binding of an ion.

Part of our current research is focused on the synthesis and application of macrocyclic receptor molecules that are able to complex selectively cations, anions or neutral molecules. For the selective complexation of potassium, benzo- and dibenzocrown ethers and hemispherand type ionophores have been synthesized [2]. In contrast to valinomycin the molecular cavity of synthetic ionophores can be tuned to the desired ion selectivity. Moreover, they can be easily functionalized which offers the possibility of covalent attachment of the ionophore to the membrane matrix [3, 4]. In this way one of the major drawbacks related to the use of plasticized PVC membranes, the leaching out of the ionophore in the sample solution, can be overcome. Detachment of plasticized PVC membranes from the gate surface, another problem for sensor lifetime, can

be prevented by covalent chemical anchoring of siloxane membranes to the surface of the gate oxide [5–8]. In combination with a chemically attached polyHEMA interlayer between gate oxide and sensing membrane a thermodynamically well-defined membrane–insulator layer interface is obtained. When adequately buffered this interlayer also suppresses interference from carbon dioxide. Previously, we have reported that a polyHEMA interlayer, conditioned in a buffered sodium chloride solution, between the gate surface and the sensing membrane was necessary to obtain satisfactory Nernstian-behaving sodium-sensitive CHEMFETs, based on calix[4]arene ketones [9].

Our further investigations of Na⁺-CHEMFETs were focused on the improvement of the Na⁺/K⁺ selectivity using calix[4]arene amides as ionophores. For comparison the sodium-selective oxamide ETH 2120 was also included in this study. The structures of the ionophores are given in Fig. 1. The ionophores were incorporated in a plasticized PVC matrix. Although this will not be the ultimate system for durable Na⁺-CHEMFETs, it still offers a simple and fast method to screen the sensing properties of a variety of calixarenes. During this study it became apparent that there is a remarkable effect of anionic sites, i.e. tetraphenylborate ions, incorporated in the membrane, towards the Na⁺/Ca²⁺ selectivity.

Experimental

Chemicals

High-molecular-weight PVC was obtained from Janssen Chimica; ETH 2120, bis(2-ethylhexyl) sebacate

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Fig. 1. Structures of the investigated ionophores.

(DOS) and potassium tetrakis(4-chlorophenyl)borate (KTCPB) were obtained from Fluka. The pH 4 buffer was purchased from Yokogawa. The synthesis of calix[4]arene amides **1** has been described previously [10], and **2** was synthesized in a similar way. Tetrahydrofuran (THF) was freshly distilled from benzophenone/sodium before use. The alkali and alkaline earth metal salts used were of analytical-reagent grade (Merck-Schuchardt), except sodium chloride (Suprapur). All solutions were made with doubly distilled and deionized water.

CHEMFETs

The ISFETs used in this study, which contained an intermediate hydrogel layer of polyHEMA between the gate oxide and the sensing membrane, were fabricated as described previously [6]. The polyHEMA layer was anchored chemically to the gate oxide as described before [4, 8]. The ion-sensitive membranes were prepared by solvent casting of a mixture composed of PVC (33 ± 1.5 wt.%), DOS (65 ± 1.5 wt.%), ionophore (2 ± 0.5 wt.%), and, if used, KTCPB (50 ± 5 mol%, with respect to the ionophore). The mixture, with a total weight of around 100 mg, was dissolved in 1 ml of THF and casted on mounted ISFETs that were encapsulated with epoxy resin (Hysol). The THF was allowed to evaporate overnight. The polyHEMA interlayer was, prior to solvent casting, conditioned by immersion in a buffered (pH 4) 0.1 M NaCl solution for 3–6 h. Before starting measurements the membranes were conditioned in 0.1 M NaCl solution for at least 4 h.

Measurements

The output of the ISFETs was measured in a constant drain-current mode ($I_d = 100 \mu\text{A}$), with a constant drain-source potential ($V_{ds} = 0.5$ V) [11]. This was achieved using an ISFET amplifier of the source-drain follower type. The developed membrane potential was compensated by an equal and opposite potential (ΔV_{gs}) via the reference electrode. A saturated calomel electrode (SCE) was used as reference with a double junction containing 1.0 M LiOAc. Ten ISFETs were monitored simultaneously and the data were collected and analyzed using the Apple IIgs microcomputer. All equipment was placed in a dark and grounded metal box to eliminate any effects from static electricity and the photosensitivity of the ISFETs. The potentiometric selectivity coefficients, K_{ij}^{Pot} , were determined by the fixed interference method (FIM) [12]. The constant background concentration of the interfering ions was 0.5 M in the case of CHEMFETs incorporating the calix[4]arene amides **1** and **2**, except for calcium for which a 0.1 M solution was used. When ETH 2120 was incorporated in the sensing membrane the measurements were performed in solutions with a constant background concentration of 0.1 M for all the interfering ions. All concentrations were converted to activities by using the extended Debye–Hückel equation [13]. The obtained response characteristics were analyzed according to the Nicolsky–Eisenman equation [14], where all the symbols have their conventional meanings.

$$E = E^0 + S \log \left[a_i + \sum K_{ij}^{\text{Pot}} a_j^{z_i/z_j} \right], \quad S = 2.303 RT / z_i F$$

Results and discussion

Experiments performed with CHEMFETs based on pyrrolidine amide **1** showed improvement of the Na^+/K^+ selectivity, i.e. $\log K_{\text{Na,K}}^{\text{Pot}} = -2.3$ (Table 1), compared to the earlier results for CHEMFETs incorporating *p*-tert-butylcalix[4]arene tetraphenylketone, which showed a $\log K_{\text{Na,K}}^{\text{Pot}}$ of -1.9 [9]. In contrast, however, the $\text{Na}^+/\text{Ca}^{2+}$ selectivity was reduced remarkably. It is known that K^+ and Ca^{2+} usually interfere strongly in Na^+ detection, because of the favourable partition of the interfering ion into the membrane phase and/or by the association constants between different cations and the ionophore having about the same order of magnitude. From measurements of stability constants (β), by Arnaud-Neu *et al.* [10], it is known that pyrrolidine amide **1** forms slightly stronger complexes with Ca^{2+} than with Na^+ in methanol, i.e. $\log \beta$ 7.8 and 7.2, respectively. This may explain the decrease in $\text{Na}^+/\text{Ca}^{2+}$ selectivity although it

TABLE 1. Response characteristics for CHEMFETs based on calix[4]arene amides **1** and **2**, and ETH 2120

Interfering ion, <i>j</i>	log $K_{Na,j}^{Pot}$ [slope/mV dec ⁻¹]					
	Ionophore					
	1	1	2	2	3	3
	Mol% KTCPB					
	50	0	50	0	50	0
Cs ⁺	≤ -4.0 [59.2]	≤ -3.9 [59.5]	≤ -4.1 [60.4]	≤ -4.2 [59.9]	-2.1 [49.7]	-2.6 [60.6]
Rb ⁺	-3.6 [59.8]	-3.7 [59.2]	-3.7 [59.8]	-3.8 [59.1]	-1.7 [55.1]	-2.2 [61.6]
K ⁺	-2.3 [58.3]	-2.3 [59.2]	-2.7 [59.2]	-2.7 [58.2]	-1.3 [58.9]	-1.6 [58.8]
Li ⁺	-2.6 [59.6]	-2.7 [57.0]	-2.7 [58.8]	-2.7 [58.4]	-1.1 [53.5]	-1.4 [58.4]
Ca ²⁺	-2.1 [60.8]	-3.6 [59.0]	-2.6 [60.7]	-3.7 [59.0]	^a	-3.2 [60.4]
Mg ²⁺	≤ -4.2 [58.1]	≤ -4.2 [58.5]	≤ -4.2 [59.5]	≤ -4.3 [59.0]	-2.8 [51.3]	-3.6 [59.4]

^aOnly minor responses of a few mV decade⁻¹ were observed.

was not expected based on the more unfavourable partition of the Ca²⁺ ion into the membrane phase.

Tetraphenylborate ions are frequently added to the membrane for known advantages, i.e. reduction of the interference by lipid-soluble anions, lowering of the electrical membrane resistance and the time response after an activity step, and lowering of the activation barrier for the cation-exchange at the membrane/solution interface [15, 16]. The latter effect, from which it can be concluded that the tetraphenylborate seems to function as an ion-transfer catalyst, induced us to examine the effect of the presence or absence of tetraphenylborate in the membrane matrix. As can be concluded, from Table 1, the absence of tetraphenylborate has no large influence on the response characteristics. The potentiometric selectivity coefficients and slopes for all interfering ions, except for Ca²⁺, are similar to the membranes which contained tetraphenylborate. However, Ca²⁺ as the interfering ion showed a remarkable improvement of the Na⁺/Ca²⁺ selectivity by a factor 32. The same experiments were also performed with CHEMFETs incorporating tetrakis(dimethylacetamide)calix[4]arene **2** as the ionophore. As can be seen, from Table 1, a similar difference in the Na⁺/Ca²⁺ selectivity was observed. Although in this case the tetraphenylborate-free membrane had only a factor 13 better selectivity. Furthermore, a very good enhancement in selectivity versus the K⁺ ion was observed, i.e. log $K_{Na,K}^{Pot} = -2.7$. This is, to our knowledge, the best value reported in ISE and FET measurements. The higher Na⁺/K⁺ selectivity of ionophore **2** compared to **1** is presumably a consequence of the smaller steric hindrance by the dimethylamino group in comparison to the bulkier pyrrolidine ring. This results in a better fit of the Na⁺ ion in the cavity. For comparison also experiments were performed with ETH 2120-based

CHEMFETs. For this ionophore the presence of the tetraphenylborate ions in the membrane matrix showed next to a decrease in sodium selectivity also a sub-Nernstian response for all interfering ions. Almost no response was observed in a sample solution of 0.1 M Ca²⁺. CHEMFETs based on ETH 2120 with a tetraphenylborate-free membrane matrix gave good responses with Nernstian behaviour; it should be noted that the values for the slopes as well as for the selectivity coefficients are considerably improved compared with the values reported earlier [9]. Moreover, the values obtained agree well with the selectivities found for Na⁺-selective electrodes by Maruizumi *et al.* [17] and Gehring *et al.* [18].

Conclusions

Whereas addition of tetraphenylborate ions to the membrane matrix generally improves the electrode characteristics it is shown in this study that it also can have unfavourable effects on its functions as an ion transfer catalyst. Incorporation of tetraphenylborate ions in a PVC membrane decreases the Na⁺/Ca²⁺ selectivity remarkably in the case of CHEMFETs based on calix[4]arene amides **1** and **2** and falls even to zero for the ETH 2120-based CHEMFETs. The Na⁺-CHEMFETs based on calix[4]arene amides **1** and **2** exhibit better selectivities, both in the presence and absence of tetraphenylborate ions in the membrane matrix, than the commercially available ETH 2120. Na⁺-CHEMFETs modified with a membrane matrix without tetraphenylborate ions, incorporating tetrakis(dimethylacetamide)-calix[4]arene **2** show a remarkable good selectivity versus all investigated interfering ions, especially noteworthy are the selectivities towards K⁺ and Ca²⁺.

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