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# Comparison of polysiloxane films substituted by undecenyl-cyclam and by naphthyl-cyclam for the design of ISFET devices sensitive to $Fe^{3+}$ ions

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## ABSTRACT

The synthesis and properties of new silicone-based functional materials having attached cyclam macrocycles have been assessed with regard to their application as ion-sensitive membranes of chemical sensors. The preparation process of thin films of the sensitive materials has been designed so that each chemical compound is attached by means of chemical bonds: the macrocyclic ionophore was chemically bound to the silicone polymer and the polymer material was attached to the sensitive surface of the electrochemical devices by means of chemical grafting. The properties of such materials have been evaluated for detection of iron(III) species in water using ion-sensitive field-effect transistor (ISFET) and electrolyte–insulator–semiconductor (EIS) structures, both sensitized by a coating with the functional polymer materials. Two types of cyclam derivatives and two types of synthesis processes have been compared with that respect. The first material, "PDMS-Cyclam", was prepared by grafting *N*-10-undecenyl-cyclam to poly(methylhydrosiloxane) (PMHS). The cyclam ionophore of the second material, "PDMS-Naphthyl-Cyclam", bore a naphthyl pendent group that enhanced the complexing properties for $Fe^{3+}$ ions. Linear response with respect to the pFe(III) = –Log[$Fe^{3+}$] was observed over three decades (EIS) or two decades (ISFET) of concentration. A Nernstian response toward $Fe^{3+}$ ions was observed for the "PDMS-Naphthyl-Cyclam" membrane. These devices exhibit good chemical stability and a long lifetime in aqueous medium.

## 1. Introduction

Iron(III) is an important metal ion in living organisms; $Fe^{3+}$ and its complexes are present in hemoglobin, myoglobin, heme enzymes and in other cofactors essential in the reactivity of biological species; it is involved in cellular energy regeneration processes [1–4]. The accumulation of large amounts of iron(III) in the body causes several heart malfunctions and may be the origin of other diseases such as cancer and haemochromatosis. Iron deficiency is the major cause of anemia in the body [5–8]. Consequently, there is a need for effective, rapid and sensitive analytical methods for detecting and monitoring iron species in clinical, medicinal and environmental media [9,10]. Several analytical techniques have been used for iron detection in biological samples such as induced coupled plasma/mass spectrometry [11], luminescence [12], voltammetry [13] and ion chromatography [14]. However, these analytical techniques face major drawbacks such as complicated pretreatment procedures and the need for heavy and sophisticated equipment that cannot be made available onsite.

In order to remedy these problems, chemical sensor technologies are considered because such devices are of small size and easy implementation for fast in-line analyses and possibly in vivo detection. Several types of potentiometric sensors for the analysis of iron(III) have recently been developed and reported [15–19].

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Among them, ion-sensitive field-effect transistors (ISFET) bearing physisorbed calixarene macrocycles as ionophore appeared particularly promising because of their favorable sensitivity for the detection of iron(III) in water [20]. Unfortunately, the lifetime of the devices was quite short because of the poor stability of the sensitive layers adsorbed at the surface of the transducer. This drawback is inherent to the sensitization technique that relies on adsorption. The ionophore slowly leaks into the aqueous medium during the measurements, causing a slow drift of its characteristics, a loss of sensitivity, and finally a short lifetime.

ISFETs are fabricated by means of microelectronics technologies that allow the mass manufacture of robust devices of small size at a low cost. The electrical specificities of such devices allow favorable characteristics of the analytical devices such as fast response times and low output impedance [21]. The design of sensitive ISFET chemical sensors is the subject of active research in the fields of supramolecular chemistry. The aim is to select complexing agents that allow specific recognition of iron(III) species [22–24], and in-surface immobilization processes to produce an ISFET surface that will be durably sensitized by strong immobilization by means of chemical grafting [25].

Macrocyclic ligands having oxygen, nitrogen or phosphorus heteroatoms form multidentate complexes that display a favorable selectivity with respect to the type of cation. Macrocycles bearing additional pendant complexing groups display an enhanced selectivity for binding metal cations [26,27]. Of these, aza-macrocycles and their derivatives are strong ligands for $Fe^{3+}$ ions [28–30]. Two cyclic tetra-amines play a key role in this field, namely cyclen (1,4,7,10-tetraazacyclododecane) and cyclam (1,4,8,11-tetraazacyclotetradecane). As an example, the stability constant of the iron-1,4,8,11-tetraazacyclotetradecane complex was high enough ($\log K = 8.9$ in 90% (v/v) DMSO/water mixed solvent) to be used as an ionophore [16]. Such macrocycles are of quite versatile application since they can be functionalized and/or attached to solid surfaces quite easily [31–37]. Several applications of their metal complexes could be developed in the medical domain including MRI contrast agents [29,30,38,39], DNA cleavers [29,40], radioimmunotherapy [41,42], and in other domains such as enzyme mimetic compounds [43,44], catalysis [45], separation and transport of gases [46,47] analytical chemistry [48,49] and extraction of metal cations [50,51]. For these reasons, cyclam is considered as a good candidate for its implementation as an ionophore in chemical sensors for the detection of iron(III). To our knowledge, it has not been used so far for the sensitization of field-effect transistors and the manufacture of ISFET devices [52]. To this end, the ionophore must be immobilized by strong binding to the transducer surface. Polysiloxane materials are effective coupling agents because of their several important properties such as biocompatibility, low toxicity, poor wettability and low surface tension [53,54]. Functionalization of the linear polysiloxane backbone can be performed by means of hydrosilylation of Si—H groups of poly(methylhydrosiloxane) (PMHS) [55–57] using a platinum catalyst. Organic functionalization of PMHS produces various materials, e.g. cross-linked materials [58], liquid crystalline [59] and drug delivery systems [60].

In the present work, the functionalization of PMHS by cyclam and cyclam derivatives has been developed and the use of the functional materials as thin ion-sensitive membrane on ISFET devices for monitoring iron(III) has been assessed. New ISFET and EIS devices based on substituted polysiloxanes bearing cyclams as lateral groups have been studied for their application to the detection of $Fe^{3+}$ ions. Two different types of functional polymers were prepared (Fig. 1): the first, called “PDMS-Cyclam”, consisted in a polymethylsiloxane backbone with cyclam macrocycles attached to one of their amino groups; the second, called “PDMS-Naphthyl-Cyclam”, contained an additional naphthalene group attached to another amino group of the cyclam. The presence of the naphthyl group enhances the complexing properties with regard to $Fe^{3+}$ ions.

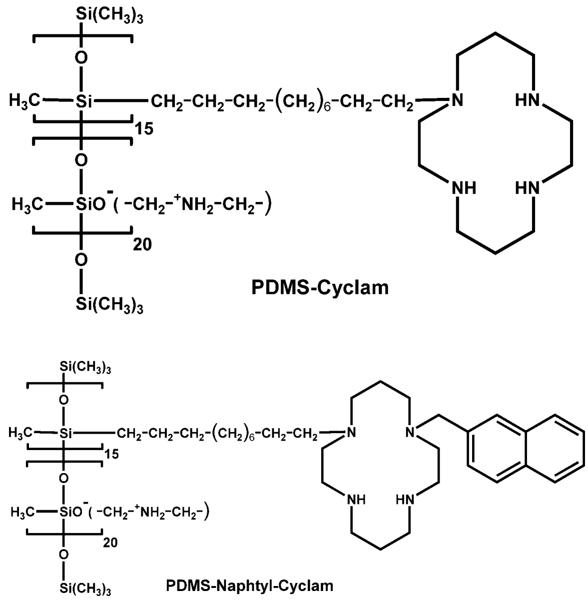

**Fig. 1.** Chemical structures of PDMS-Cyclam and PDMS-Naphtyl-Cyclam.

## 2. Experimental

### 2.1. Reagents and materials

Cyclam (1,4,8,11-tetraazacyclotetradecane) was purchased from CheMatech (Dijon, France); it was stored in a vacuum desiccator because of its high sensitivity to moisture. PMHS from ABCR was stored in the refrigerator in order to avoid any hydrolysis followed by polycondensation reactions of the hydrosilane groups. 10-Undecenyl bromide 95%, 2-(bromomethyl)naphthalene and the hydrosilylation catalyst platinum(0)-1,3-divinyl-1,1,3,3-tetramethyldisiloxane complex (PDTD) 3% in xylene (Karstedt’s catalyst) were from Sigma–Aldrich. 2-(bromomethyl)naphthalene was used with caution under a hood because of its high toxicity. Chloroform was dried by distillation at atmospheric pressure. Dimethylformamide was distilled under reduced pressure in the presence of $P_2O_5$ before storage under dry conditions. Analytical grade iron nitrate and ammonium acetate were purchased from Sigma–Aldrich.

The potentiometric measurements were carried out with ISFETs produced at the National Center of Microelectronics of Barcelona (Spain). The ISFETs were made of a positively doped silicon substrate in which were located two n-doped areas (the drain and the source, to which were applied two metal electrodes). The central area of the transducer between the drain and source (channel) was top-coated by a thin insulating layer of $SiO_2$ covered by a layer of $Si_3N_4$ that significantly improved the signal-to-noise ratio.

The Au/Ti/pSi/$SiO_2$/$Si_3N_4$ substrates were supplied by the technology center LAAS-CNRS (Toulouse). They were based on p-type silicon wafers. Thin layers of thermally grown silicon dioxide (50 nm) and silicon nitride (100 nm) were generated on the surface of silicon plates by low pressure chemical vapor deposition (LPCVD) technique. The electrical contacts were realized by deposition of a gold film (200 nm) on the backside of the wafers. The Au/Ti/pSi/$SiO_2$/$Si_3N_4$ electrodes used as transducers had an active surface of about 0.3 $cm^2$ where the chemical sensitization was performed.