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A reference-less semiconductor ion sensor

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ABSTRACT

Ion sensing represents a grand research field with tremendous challenges and ample opportunities. A proper operation of ion sensors demands a robust reference electrode (RE), but on-chip integration of a conventional liquid-filled RE is incompatible with semiconductor technology for manufacturing ion-sensitive field-effect transistors as electronic sensors. Here, we demonstrate a reference-less semiconductor ion sensor, RELESIS, that integrates an interdigitated electrode (IDE) with a field-effect transistor. As a constant solution potential is no longer necessary, the use of RELESIS eliminates the need of any RE in ion sensing. The evaluated IDE comprises two intertwined metallic combs, each being covered with a specific sensing layer. One of the combs is connected to the transistor for readout while another is biased with a voltage signal source. Our extensive measurement results with pH sensing confirm that the sensitivity of RELESIS is exclusively determined by the sensitivity difference of the two sensing layers. By eliminating bulky REs, the RELESIS may find myriad ion-sensing applications owing to its miniaturisability, integrability, flexibility and cost advantages.

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1. Introduction

Ion sensors are generally potentiometric meters that correlate the electrical potential difference at a solid/liquid interface to the ion concentration to be determined in a solution [1,2]. Glass electrodes based on conducting glasses that are able to detect hydrogen ion concentrations were developed a century ago [3]. A typical modern commercial pH (hydrogen ion) sensor usually integrates a glass electrode for sensing and a reference electrode (RE) for setting the potential standard into one single device [4–6]. A widely used Ag/AgCl RE consists of a chlorinated Ag wire soaked in a KCl saturated solution thereby making a complete redox cell in order to attain a stable solution potential difference. pH sensors with such a glass electrode along with a bulky Ag/AgCl RE are in daily use at laboratories of chemical and physiochemical analyses [3,7–9].

However, the Ag/AgCl RE is difficult to miniaturize to micrometre-size dimensions that can match the size of an ion-sensitive field-effect transistor (ISFET) electrode [10]. Its fabrication is incompatible with semiconductor technology used for manufacturing ISFETs. An ISFET represents an electronic sensing electrode increasingly replacing the traditional glass electrode for precision

pH measurement. It is essentially a tailor-made FET with its gate metal-electrode being replaced by an aqueous solution containing the ions to be quantitatively measured. When ions (such as H^+ for pH sensing) are adsorbed on the ISFET sensing surface, the sensing layer/solution interface potential is altered. Consequently, the channel conductance and thereby the transistor current are changed. An RE, despite often being bulky and fragile, is, however, still indispensable as the electrical potential of the measured aqueous solution needs to be kept constant during ion sensing.

Since the invention of ISFET by Piet Bergveld in 1970 [10,11], the FET-based ion sensors have been extensively studied for detecting hydrogen and other ions as they offer superb robustness, exceptional miniaturization capability, fast response and great potential for in vivo clinical analyses [11]. The vast development of integrated circuits based on complementary metal-oxide semiconductor (CMOS) technology [12–17] has enabled the implementation, based on the pH sensing principle, of ultrahigh-density integrated sensor arrays for genome sequencing [18–21] and quantitative DNA amplification by means of polymerase chain reaction [22–24]. An on-chip or even a beside-device reference electrode (RE) is highly desirable in order to set a precise and stable potential reference to the ISFET-measured solution [11]. A conventional, bulky liquid-filled RE evidently cannot meet the requirements for the desired integration with an ISFET. As a compromise, inert metals such as Pt and Au have been used as a pseudo-RE, but their interface
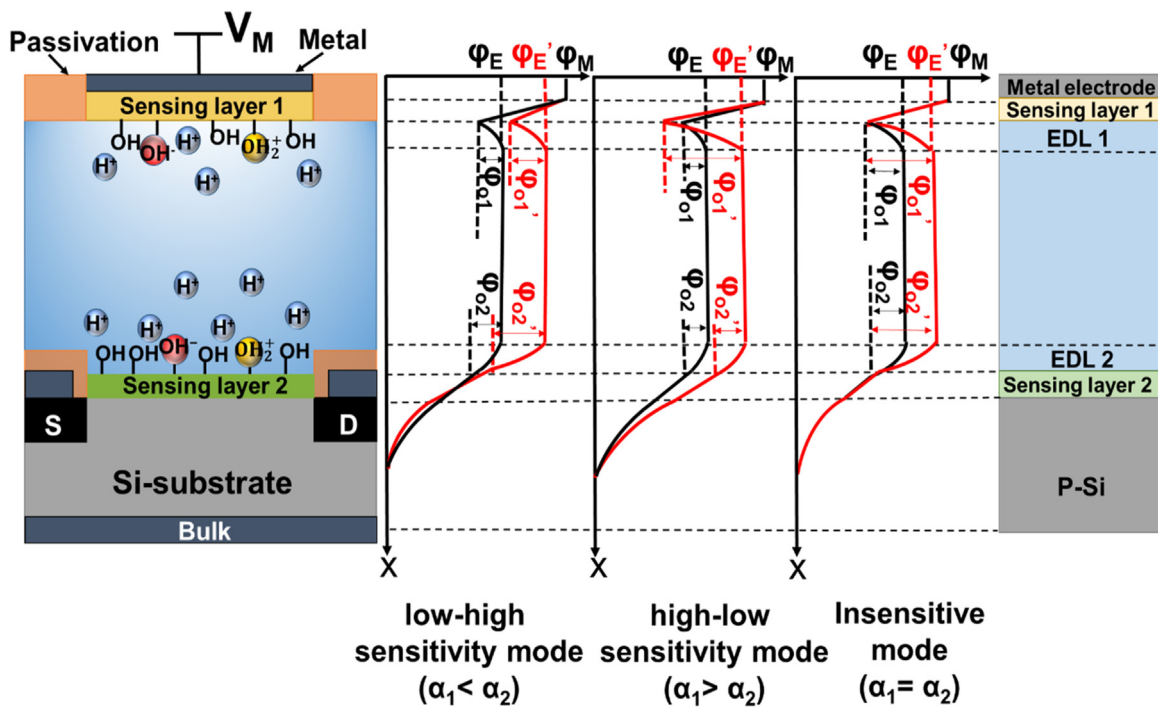

Fig. 1. Concept of RELESIS and its working principle. The schematic representation of RELESIS for pH sensing along with the potential distribution before (black line) and after (red lines) a pH increase of an exemplary n-channel RELESIS corresponding to three sensitive/insensitive modes when the surface of the semiconductor (silicon) substrate is in strong inversion. The three modes are low-high sensitivity mode ($\alpha_1 < \alpha_2$), high-low sensitivity mode ($\alpha_1 > \alpha_2$) and insensitive mode ($\alpha_1 = \alpha_2$). (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

to solutions is virtually unstable electrochemically [25,26]. Hence, the potential of the bulk solution cannot be kept constant with pH change. Research efforts have also been dedicated to combining an ISFET and an electrically identical reference FET, i.e. REFET, with a simple pseudo-RE often in the form of an evaporated Pt layer [27]. Upon careful surface treatments, the REFET is hoped not to respond to variations of the ion concentration to be measured as its sensing surface is made insensitive to the ions [28–31]. Such an approach generally suffers from several issues such as the great difficulty in making the REFET electrically identical to the sensing ISFET, the REFET and ISFET not always in tune or in equilibrium with the test solution [32], and chemical modifications of the sensing layer surfaces usually not compatible with standard semiconductor processing thus unable to satisfy the long term stability requirements [31,33]. Though some studies have reported the methods using the solid state reference electrode [34] or back gate electrode [35], they also suffer from incompatibility with semiconductor fabrication technology and reliability issues. Finding a robust integretable RE remains the most crucial issue for FET-based ion sensors. It has been urgently hoped that the challenges with RE can be overcome by inventing new FET-like ion sensing devices even without an RE [11].

In this paper, we report a proof-of-concept reference-less semiconductor ion sensor (abbreviated as RELESIS) that fundamentally eliminates the need to maintain a constant solution potential and thus the need to include an RE. The working principle of RELESIS is presented and subsequently validated with a prototype device via pH sensing. With the elimination of the cumbersome RE, this new FET-based RELESIS is compatible with semiconductor process technology and, hence, can be easily down-sized and on-chip integrated. The potential of manufacturing an ultra-compact and ultra-low cost RELESIS can facilitate biomedical applications such as in vivo clinical analyses.

2. Materials and methods

2.1. Working principle of the RELESIS

The schematic representation of RELESIS and its working principle are shown in Fig. 1 and explained as follows. In contrast to using an RE to maintain a constant bulk solution potential in a conventional ISFET, RELESIS relies on measuring the potential difference of the two face-to-face sensing layers, see below. The metallic gate electrode is supposed to be placed close enough to the FET so that its potential can control the operation of the FET. Hence the potential applied to the metallic gate electrode, V_M, covered by a different sensing layer (upper part) than that of the FET (lower part) determines the working region of RELESIS. It should be noted that both sensing layer 1 and sensing layer 2 are in a dielectric way in contact with the solution, and thus only non-faradaic process [36] can take place at the sensing layer surfaces. This is obvious for the sensing layer 2 since it is connected to the FET which has a gate insulating layer. For the sensing layer 1 of RELESIS, the prerequisite is that it is a dielectric layer or composed of stacked layers incorporating minimum one insulating layer, thus preventing faradic process. The design of RELESIS also implies that the potential of bulk solution (φ_E) is no longer constant and can vary with pH change, since the pH value of the solution determines the charge at both sensing layer surfaces and thus affect the shape of the potential profile. This property is clearly depicted in Fig. 1, which illustrates exemplary potential distribution profiles before (black line) and after (red lines) a pH increase.

According to the site-binding model (SBM) [37–41] and the electrical double layer (EDL) theory [42], the interfacial potentials established at the two face-to-face sensing-layer/solution interfaces (denoted as φ_{o1} and φ_{o2}, respectively) are opposite in polarity [40]. Similar to that of an ISFET [11], the variations of φ_{o1} and φ_{o2} caused by pH change can be expressed as $\Delta\varphi_{o1} = \varphi'_1 - \varphi_1 = -2.3\alpha_1 \frac{RT}{F}\Delta pH$ and $\Delta\varphi_{o2} = \varphi'_2 - \varphi_2 = -2.3\alpha_2 \frac{RT}{F}\Delta pH$ respectively,