

A Solid-state Potassium Ion Sensor From Acrylic Membrane Deposited on ISFET Device

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Abstract: A potentiometric K⁺ ion sensor made from chemically modified field effect transistor (K-CHEMFET) by depositing a K⁺ ion-selective membrane on ion-selective field effect transistor (ISFET) has been successfully developed. The oxide materials of ISFET gate were silicon nitride (Si₃N₄) and silicon dioxide (SiO₂). The K⁺ ion-selective membrane was a polymeric material from plasticiser-free poly(n-butyl acrylate) (nBA), which contained valinomycin acting as an ionophore and a lipophilic additive improving the membrane resistance. The K-CHEMFET characterization included a study on the effect of buffer solution, selectivity, effect of light and temperature, hysteresis, response time and sensor drift. The solid-state K⁺ ion sensor demonstrated sensitivity of 57.8±0.9 mV/decade with dynamic linear range from 0.01 to 100 mM (R²=0.9949) and detection limit of 0.003 mM of K⁺ ion. Besides, the repeatability and reproducibility of K-CHEMFET were 1.55 RSD % (Relative Standard Deviation) and 4.28 RSD % respectively.

Keywords: potentiometric sensor, valinomycin, acrylate, ion-selective field effect transistor, plasticiser-free

Introduction

ISFET is an integrated circuit which built from ion-selective electrode (ISE) and microelectronic technology (1). It is a derivation of metal oxide semiconductor field effect transistor (MOSFET). Therefore, operation of ISFET can be explained by its electrical analogue MOSFET as both devices shared similar electrical circuit. However, the main difference between ISFET and MOSFET is the ISFET gate connection is separated and modified to form a reference electrode (2).

Generally, an ISFET gate is made of gate insulator (Si₃N₄) and gate oxide (SiO₂). Sometimes it can be a metal oxide such as aluminium oxide (Al₂O₃) or tantanium pentoxide (Ta₂O₅) (3). The entire MOSFET gate is enclosed completely while only parts of ISFET (source, drain and edges of gate) are covered so as to leave the gate oxide expose to sample solution (1, 4). When the reference electrode and an ISFET are immersed in an aqueous solution, sample contact with the gate insulator/gate oxide layer is established. Response potential of ISFET arises from the detection of ion activity differences, which plays a role in supplying voltage at ISFET gate and changing current from source to drain (5, 6).

Metal oxide at the gate functions as a chemical sensing material whilst the transistor acts as a signal transducer. ISFET based sensors offer short response time, high sensitivity, micro-sized and can be employed for simultaneous detection of multiple

species. However, ISFET electrode does not appear in market until the early of 1990 after its invention of 20 years. This is due to the inability to resolve the drift and instability problems caused by the lacking of good ISFET encapsulation technology (7).

ISFET gate typically sensitive towards pH change but can be made sensitive towards other ion species by putting a layer of membrane which contains the desired ion-sensitive molecule on the ISFET gate (8). Ion-selective membrane based ISFET also known as CHEMFET (3). K⁺ ion sensor based on CHEMFET or K-CHEMFET has been well studied as an ISFET based sensor. However, several common problems faced by these ion sensors were leaching of ionophores from the immobilization matrix and detachment of membrane layer from the ISFET sensing area. This is particularly so when a conventional membrane such as poly(vinyl chloride) (PVC) is applied as the ionophore immobilization membrane matrix. It is also the main cause of ISFET ion sensor for having short life span (6, 7, 9, 10).

In order to resolve such problems, various polymers have been employed as membrane material in the fabrication of ISFET ion sensor. Nevertheless, the need of plasticiser in certain polymers is inevitable, which weaken the adhesion of the membrane to ISFET gate and this lengthen the response time. Although the use of modified membrane with polysiloxane is capable in coping with some of these problems, it is difficult to synthesize and not commercially available (10). Polyimide and polymethacrylate are examples of

membrane material with own good adhesive property and widely used as membrane matrix (7). Photocured polymer is another popular material in the fabrication of ISFET ion sensor. It is because photopolymerisation allows polymer membrane to be formed directly on the transducer with possible surface covalent binding if the polymer is functionalized (11).

The aim of this study was to fabricate a solid-state K-CHEMFET by applying photocurable and plasticiser-free poly(nBA) as ion-selective membrane. The main advantage of this membrane material is good adhesion on solid surface and no leaching of membrane component such as ionophore. The preparation of K-CHEMFET using this polymeric material is simple and rapid.

Materials and Methods

Materials

The development of K-CHEMFET sensor involved chemicals such as: 2,2-dimethoxy-2-phenylacetophenone (DMPP), sodium tetrakis [3,5-bis (trifluoro-triethyl) phenyl] borate (NaTFPB), potassium ionophore (valinomycin), magnesium chloride ($MgCl_2$) obtained from Fluka. Sodium hydroxide (NaOH), potassium chloride (KCl), sodium chloride (NaCl) purchased from System. Also, n-butyl acrylate (nBA) from Merck, 2-hexanediol diacrylate (HDDA) from Sigma Aldrich, Tris(hydroxymethyl) aminomethane (Tris-HCl) from DUCHEFA BIOCHEMIE, ammonium chloride (NH_4Cl) from Ajax Chemicals, calcium chloride ($CaCl_2$) from Hamburg Chemical, hydrochloric acid 37 % (HCl) from Riedel-de Haen. All chemicals used were of analytical grade and without further purification. All chemical solutions were prepared with deionised water.

Fabrication of K-CHEMFET sensor

K^+ ion-selective membrane cocktail was prepared for the fabrication of K-CHEMFET were as reported elsewhere (12) and modified a little in this experiment. An monomer (nBA) stock solution was

prepared by mixing 950 μL nBA and 1 μL cross-linker HDDA. A mixture of 0.8 mg lipophilic salt NaTFPB, 1 mg DMPP and 1.9 mg K^+ ionophore was then added 100 μL of the nBA stock solution. The cocktail was stirred until homogen and later kept at 4 $^{\circ}C$ when not use. A thin plastic ring was adhered onto the ISFET gate (ISFET device from Malaysian Institute of Microelectronic Systems, MIMOS) and leaving the gate oxide exposed. The purpose of the ring was to confine and control the membrane thickness at the gate oxide. 3.5 μL cocktail drop-coated onto the ISFET sensing area and then photocured in a ultraviolet (UV) radiation unit (R.S. Co) for 180 s under nitrogen gas purging. The K-CHEMFET design in this study is shown in Figure 1.

Evaluation of K-CHEMFET sensor response

The response of the K-CHEMFET (output voltage, V) was tested in a series of potassium chloride (KCl) solutions with concentration 10^{-1} – 10^{-8} M. During the measurements, K-CHEMFET and Ag/AgCl reference electrode were connected to a circuit board (from MIMOS) containing a power generator (Protek DC Regulated Power Supply). The sensor response was recorded when a stable reading was demonstrated by the multimeter (Fluke 177). The response measurements of the K-CHEMFET were performed in triplicates.

The effect of pH and Tris-HCl buffer towards K-CHEMFET response was investigated with a series of 10 mM Tris-HCl buffer at a pH range of 4–10. To determine the potentiometric selectivity coefficient ($\log K_{A,B}^{pot}$) of the sensor, five different 0.1 M chloride solutions were prepared including KCl, NaCl, NH_4Cl , $CaCl_2$ and $MgCl_2$ where the selectivity behaviour towards these cations was evaluated using the separate-solution method (SSM). SSM involved potential measurement of a cell which consisted of the K-CHEMFET and a reference electrode in several different (interference) ion solutions separately. Concentrations of all interfering ions and K^+ ion shared the same ion activity.

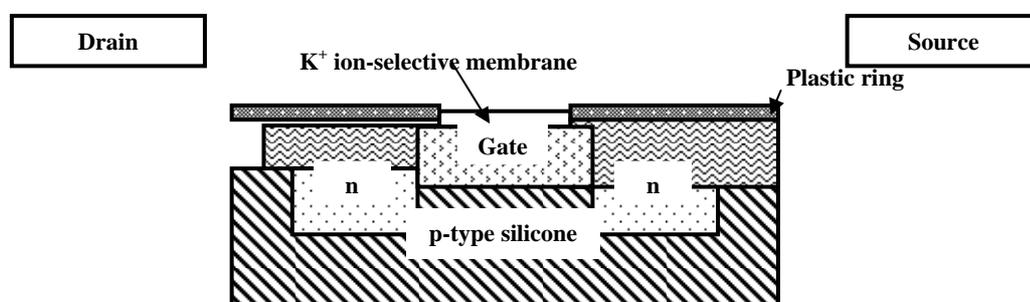


Figure 1: K-CHEMFET design in this study.

The effect of light on the K-CHEMFET gate response was assessed in bright and dark conditions using KCl standard solutions (0.1–100 mM). For the

temperature effect, K-CHEMFET was tested with three series of KCl solutions (0.1 M, 0.01 M and 0.001 M) separately under temperature gradually increased from

26 °C to 30 °C. The response was recorded at every increment of 1 °C. For the hysteresis test, a series of KCl standard solutions with concentration ranged from 10^{-1} – 10^{-8} M were used. Initial response of the K-CHEMFET in a KCl solution was taken at 0 min and followed by second reading after 5 min. Both sensor and reference electrode were rinsed with deionised water before the response of a new K^+ ion concentration was measured. The procedure was repeated for all other concentrations of K^+ ion.

The response time of K-CHEMFET also investigated in KCl standard solutions (10^{-1} – 10^{-8} M), where the output voltage value was taken at every 5 s from the start of the measurement until a stable reading was obtained. Response time was determined when the variation of the output signal is less than 5 %. For the drift test, K-CHEMFET and reference electrode were immersed in 10 mM KCl solution and the output voltage was recorded every hour for a total of eight hours.

Results and Discussion

Response of blank-ISFET towards pH

Blank-ISFET is sensitive to H^+ ion concentration and produces signal according to the activity of proton at the sensing gate. ISFET shares similar electrochemistry behaviour with ISE where change of electrode potential against analyte activity obeys the Nernst equation (1, 3). Figure 2 demonstrated that the blank-ISFET responds linearly towards H^+ ion concentration in Tris-HCl buffer with sensitivity of 55 mV/decade ($R^2=0.9959$). The sensitivity of ISFET was near to Nernstian slope.

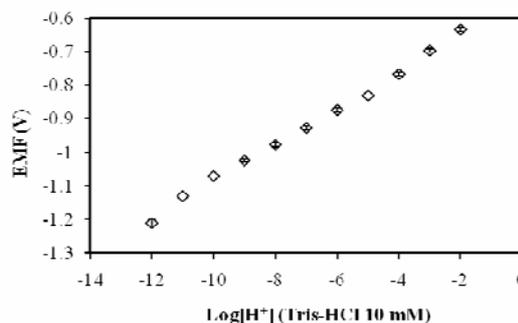


Figure 2: Response of blank-ISFET in Tris-HCl buffer solutions.

Response of K-CHEMFET

The response of CHEMFET is based on the potential changes at the membrane/aqueous interface due to the formation of K^+ -transporter complex at the border of the external phase. The total H^+ ion diffuse from the ion-selective membrane to the outer layer of the membrane is the same as the total K^+ diffuse into the membrane. Therefore, the CHEMFET transducer also responds to H^+ ion flow at the inner membrane interface (1, 3).

The K-CHEMFET fabricated in this study exhibited a linear response range to K^+ ion from 0.01–100 mM and a sensitivity of 57.8 ± 0.9 mV/decade ($R^2=0.9949$) with lower detection limit of 0.003 mM (Fig. 3). The sensitivity is near to Nernstian slope (59.16 mV/decade) and this demonstrated that the membrane adhesion was compatible with the sensing gate. The absence of plasticiser and the ability to effectively immobilised membrane materials (K^+ ionophores and NaTFPB lipophilic salts) in the poly(nBA) network reduces leaching problem and these are the reasons for a good K-CHEMFET response (13, 14). The relative standard deviation (RSD) of the sensor was less than 5%. (Table 1).

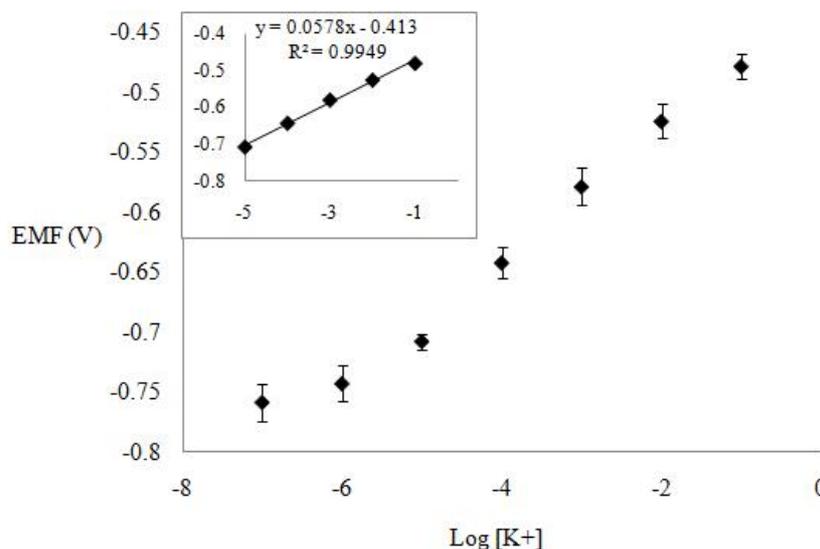


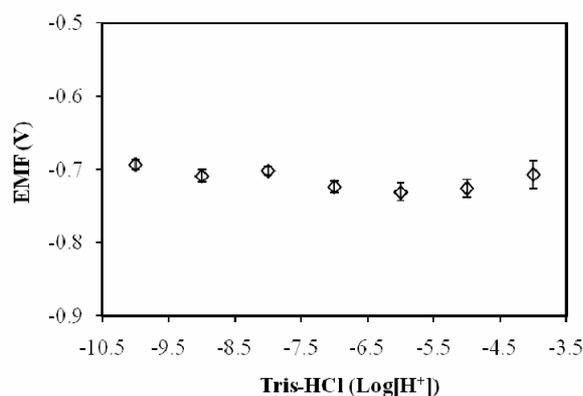
Figure 3: The response of K-CHEMFET in a series of standard KCl solutions (10^{-1} – 10^{-8} M).

Table 1: Analytical performance of K-CHEMFET in K⁺ ions.

| Parameters | K-CHEMFET |
|---------------------------|-----------|
| Sensitivity (mV/decade) | 57.8±0.9 |
| R ² | 0.9949 |
| Dynamic linear range (mM) | 0.01–100 |
| Detection limit (mM) | 0.003 |
| Repeatability (RSD %) | 1.55 |
| Reproducibility (RSD %) | 4.28 |

Effect of Tris-HCl buffer on K-CHEMFET

The K-CHEMFET did not yield response when tested in a series of 10 mM Tris-HCl buffer solutions at different pHs (Fig. 4). The movement of H⁺ ion across the membrane phase in the absence of H⁺ ionophore was blocked. Therefore, in the presence of a K⁺ ion-selective membrane, the ISFET gate is not sensitive towards pH changes but only responded to K⁺ ion (Fig. 3), where the K⁺ ion moved across the poly(nBA) film with the help of K⁺ ion carrier, i.e. the valinomycin ionophore. Thus, free H⁺ ion did not involve in the response mechanism of the K-CHEMFET (3, 7).

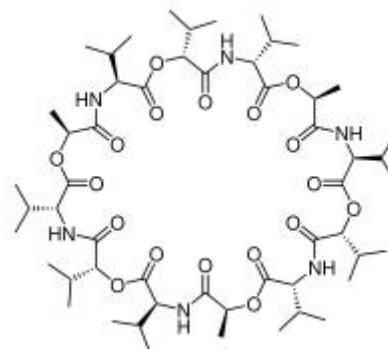
**Figure 4:** The response pattern of K-CHEMFET when exposed to different pH values of a Tris-HCl buffer.*Interference and potentiometric selectivity coefficient (Log K_{A,B}^{pot}) of K-CHEMFET*

Separate Solution Method (SSM) was applied to determine the potentiometric selectivity coefficient (Log K_{A,B}^{pot}) of K-CHEMFET where the selectivity towards each of the interfering ion can be calculated according to the Nicolski-Eisenman equation 1 (15).

$$\text{Log } K_{A,B}^{\text{pot}} = \frac{(E_B - E_A) z_A F}{RT \ln 10} + (1 - z_A/z_B) \text{Log } a_A \dots (1)$$

| | |
|-------------------------------------|--|
| Log K _{A,B} ^{pot} | Potentiometric selectivity coefficient of interference ion B against primary ion A |
| E | Cell potential difference |
| R | Gas constant, 8.314510 JK ⁻¹ mol ⁻¹ |
| T | Temperature (K) |
| F | Faraday constant, 9.6485309x10 ⁴ Cmol ⁻¹ |
| a _A | Activity of primary ion A |
| a _B | Activity of interference ion B |
| z _A | Charge of primary ion A |
| z _B | Charge of ion B |

K-CHEMFET is selective towards K⁺ ion compared to other cations because valinomycin (Fig. 5) was used as the ionophore. Valinomycin is a dodecadepsipeptide that consists of 12 amino acids and esters, which arranges in an alternate manner to form a macrocyclic molecule. Valinomycin works as a specific transporter for K⁺ ion by assisting the movement of K⁺ ion across the membrane from bulk solution to ISFET gate. Thus, K-CHEMFET exhibited large response when K⁺ ion present in sample solution (16).

**Figure 5:** The structure of valinomycin, a K⁺ ionophore.

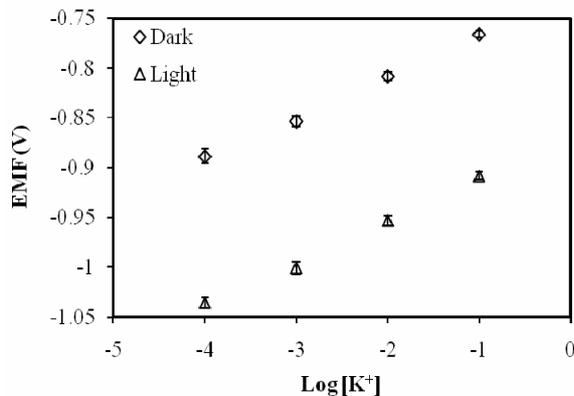
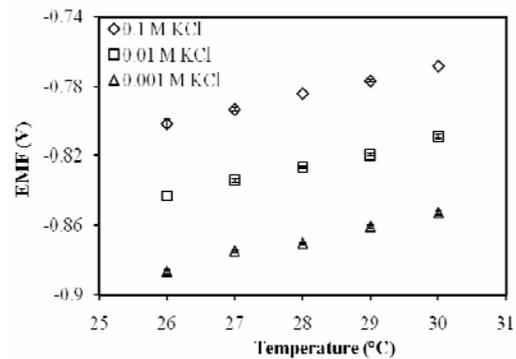
An increasing negative value of the Log K_{A,B}^{pot} indicates a lesser affinity of an ion in interfering with the sensor response towards K⁺ ion. From Table 2, Mg²⁺ ion was the least interfering ion towards the response of K-CHEMFET due to the small size of Mg²⁺ ion, which is too loose to fit into the valinomycin ring and causing an unstable complex. This is followed by Na⁺ and Ca²⁺ ions, which have bigger size than Mg²⁺ ion but still smaller size when compared to K⁺ ion. The stability constant for the potassium-valinomycin complex is 10⁶ while the sodium-valinomycin complex was only 10, hence K⁺ ion is preferred over Na⁺ ion. For NH⁺ ion, it appears to exert interference on the sensor response. This is because the size and charge of NH⁺ ion are almost the same as that K⁺ ion (16).

Table 2: K-CHEMFET selectivity towards four different cations.

| Ion (0.1 M) | Log $K_{A,B}^{pot}$ |
|------------------------------|---------------------|
| Na ⁺ | -3.461 |
| NH ₄ ⁺ | -1.713 |
| Ca ²⁺ | -3.290 |
| Mg ²⁺ | -4.862 |

Effect of light and temperature towards K-CHEMFET response

A change of light and temperature can affect the ISFET behaviour. Study on the light and temperature effects is crucial especially when ISFET sensor is built for measuring an analyte in samples under an actual environment where the conditions change continuously. A change of light and temperature can cause a change in the sensor response and hence this affects the calibration curve. From Figures 6 and 7, K-CHEMFET sensitivity was not influenced by light or temperature but the actual potential measured (EMF) shifted to higher values when the K-CHEMFET was tested in dark conditions or at higher temperatures.

**Figure 6:** The Effect of light towards a K-CHEMFET response.**Figure 7:** The effect of temperature towards a K-CHEMFET response.

The observed changes are caused by the design of the ISFET gate, which does not totally enclosed by an insulating epoxy layer. Exposure of ISFET gate to light and temperature causes threshold voltage to shift where small change in the concentration of electron carrier occurs in the semiconductor of the FET device. Shift of threshold voltage is the effect of induced light or induced temperature (17). In this work, characterizations of K-CHEMFET were conducted at room temperature (25 °C) and in a dark room.

Sensor hysteresis and response time

Hysteresis is defined as the maximum changes of K-CHEMFET response for measuring the same concentration of analyte repeatedly after measuring a different concentration of KCl. According Yin and Hsiung (17), ISFET with gate oxide Ta₂O₅ and Al₂O₃ exhibited hysteresis of 0–4.4 mV. Hysteresis response of a K-CHEMFET was comparable (0–3 mV) when determined in a range of KCl solutions as shown in Figure 8.

Low values of hysteresis imply that the ion-selective membrane can efficiently transfer K⁺ ion from solution to the gate surface and also effective protonation and deprotonation process at the interface of the inner membrane and the gate oxide (17). Good efficiency of the ion transfer process of the ionophore and gate oxide explains the fast response time of K-CHEMFET, which is typically less than 5 s in this study. In addition, the high selectivity of K⁺ ionophore also assists in shorten the response time by capturing K⁺ ion at a faster rate (4, 7).

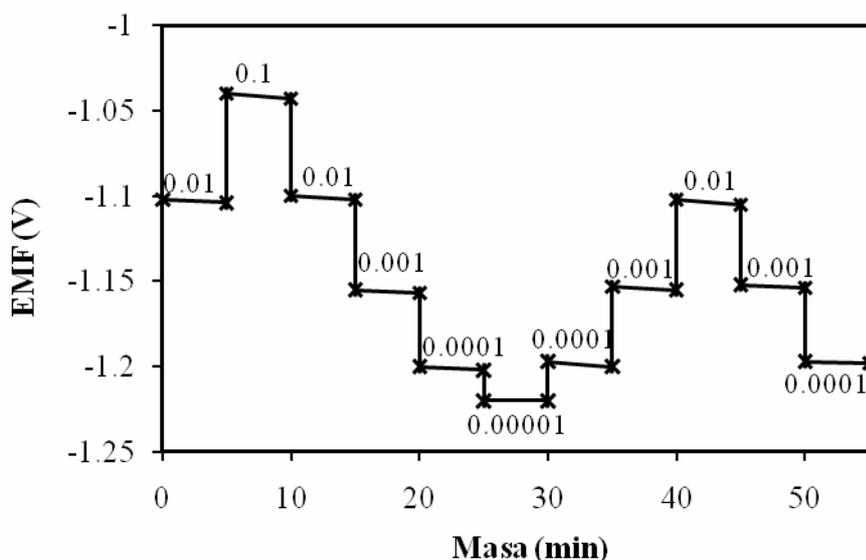


Figure 8: The hysteresis behaviour of a K-CHEMFET.

The characteristic of drift of K-CHEMFET

Tests on drift conducted for eight hours indicated that the K-CHEMFET has a drift rate of 0.02 V/hr (Fig. 9). Sensitivity patterns of K-CHEMFET before and after tests were 50.3 mV/decade ($R^2=0.9963$) and 48.1 mV/decade ($R^2=0.9726$) respectively. During immersion of the sensor, condition at the gate-solution interface is electrochemically imbalance. Such condition enhances the electric field, which then increases the ion movement within the gate-solution. Therefore the drift rate at the first three hours was large (0.04 V/hr) and later declined until the electrochemical equilibrium at the interface was reached. Moreover, huge drift rate is not merely due to external factors (e.g. interfering charge) but can be caused by the deterioration of immobilization matrix or ISFET mechanical component (17). However, sensitivity of K-CHEMFET was less affected after immersed in sample solution for a long period as the membrane adhesion and immobilization of K^+ ionophore in poly(nBA) film were good.

A comparison with reported K-CHEMFET

Several K-CHEMFETs based on various polymer matrixes as ion-selective membranes have been reported. The types of polymers studied were poly(vinyl chloride) (PVC) (3, 7, 11), polyurethane (9, 18), urushi (6), polymethacrylate (11) etc. Polymer matrix used has great influences on the sensor response. Analytical performance of poly(nBA) based K-CHEMFET in this study was better compared to other SiO_2/Si_3N_4 gate K-CHEMFET and was comparable with Ta_2O_5 or Al_2O_3 gate K-CHEMFET (Table 3). In short, gate surface also influence the sensitivity and stability of a FET based sensor. Different gate oxide has varying amphoteric sites, which play a role in the protonation and deprotonation process. ISFET gate oxide used in this study was SiO_2/Si_3N_4 , however gate surface with Ta_2O_5 or Al_2O_3 substance is considered to be better as both Ta_2O_5 and Al_2O_3 have higher amphoteric sites that can increase the buffering capacity (2, 19).

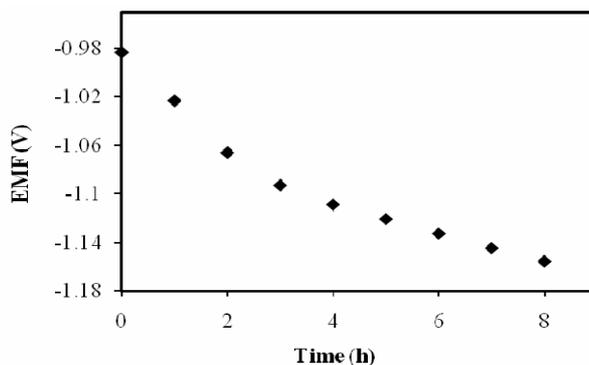


Figure 9: The drift pattern of a K-CHEMFET over a period of time.

Table 3: A comparison of analytical performance of K-CHEMFETs.

| K-CHEMFET | Gate | Membrane | Ionophore | Sensitivity (mV/decade) | Dynamic Linear range (mM) | Detection limit (mM) | Response time (s) |
|---------------------------------------|--|--|-------------|----------------------------|---------------------------------|----------------------------|-------------------------|
| This study (2010) | SiO ₂ /Si ₃ N ₄ | Poly(n-butyl acrylate) (nBA) | Valinomycin | 57.8±0.9 | 0.01–100 | 0.003 | < 5 |
| Artigas et al. (2002)[7] | Si ₃ N ₄ | Urethane diacrylate oligomer | Valinomycin | 56 | --- | --- | --- |
| Moschou & Chaniotakis (2001)[3] | Al ₂ O ₃ | Poly(vinyl chloride) (PVC) | Valinomycin | 58.5±0.6 | --- | --- | --- |
| Abramova et al. (2000)[9] | SiO ₂ / Ta ₂ O ₅ | Urethane diacrylate oligomer | Valinomycin | 56–58 | 0.01–1000 | 0.003 | --- |
| Kolytcheva et al. (1999)[11] | SiO ₂ /Si ₃ N ₄ | PVC and n- (ethyleneoxide) dimetharylate | Valinomycin | 54.0±1.5 | --- | 0.15 | --- |
| Park et al. (1996)[10] | Si ₃ N ₄ | PVC-vinyl acetate | Valinomycin | 56 | --- | --- | 1–2 |
| Wakida et al. (1988)[6] | Si ₃ N ₄ | Urushi | Valinomycin | 50 | 0.1–1000 | --- | < 10 |

Conclusion

K⁺ ion sensor based on ISFET was successfully fabricated. Application of acrylic polymer as ion-selective membrane was suitable for ISFET ion sensor. Evaluation of K-CHEMFET showed that the ISFET possessed good analytical performance and was appropriate for CHEMFET fabrication. Effects of buffer, pH and cations do not affect the K-CHEMFET response. But ISFET based K-CHEMFET still sensitive towards the changes of light and temperature. Hysteresis studies indicated that the gate oxide of ISFET was efficient in terms of protonation and deprotonation. The little drift observed from the K-CHEMFET sensor demonstrated that no major ionophore leaching and detachment of K⁺ ion-selective membrane from ISFET gate. Thus, the hydrophobic, strongly adhesive and plasticiser-free poly(nBA) is an excellent membrane material for development of ISFET based sensing devices.

Acknowledgments

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