ISFET-Based Differential pCO$_2$ Sensors Employing a Low-Resistance Gas-Permeable Membrane

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A new type of ISFET-based differential pCO$_2$ sensor system is devised by employing a low-resistance gas-permeable membrane. Both the pCO$_2$-FET and the reference FET (REFET) are made by coating their gate surfaces with an RTV silicone rubber film doped with valinomycin. The pCO$_2$ FET is covered with a hydrogel-based recipient layer inside the gas-permeable RTV membrane, but the REFET does not include the hydrogel layer. Because of low resistance of the gas-permeable membrane, the reference electrode can be placed outside as a common reference for both FETs. Output signals from the pCO$_2$-FET and the REFET are measured against the common reference, and the difference of these two signals is measured through a differential amplifier; therefore, calibration drifts of the two identical base ISFETs, caused by their thermal sensitivity, for example, cancel out. It is also shown that the ion response or the potential drifts caused by both parts of the RTV membranes cancel out exactly the same way as in the case of the base ISFETs.

A variety of chemical sensors have been devised by using pH-sensitive field effect transistors (pH-FETs) as base transducers. Such sensors include polymer membrane-coated ISFETs,[1−5] enzyme-immobilized ENFETs,[6−8] and gas-permeable membrane-coupled gas-sensing FETs.[9−12] These devices could offer the advantages of miniaturization, the capability of including multiple sensors on a single chip, integration of signal processing circuitry, and mass fabrication for cost reduction.

Previously, ISFET-based gas sensors[9−12] have been devised by employing the Severinghaus configuration, as in conventional gas sensors. For instance, a miniature pCO$_2$ sensor consists of a pH-ISFET and a thin-film Ag/AgCl reference electrode (Figure 1A). Both the ISFET and the reference electrode are covered by a hydrogel containing a bicarbonate solution. The hydrogel is then separated from the sample by a polysiloxane membrane, which is permeable to carbon dioxide. The CO$_2$ molecules diffuse through the membrane into the hydrogel layer, and the resulting pH change is detected by the pH-ISFET.

The electrical resistance of gas-permeable membranes previously employed in the Severinghaus type sensors is typically very high. As a result, a reference electrode is placed beside a pH sensor inside a gas-permeable membrane to complete an electrical measuring circuit (see Figure 1A). Therefore, the fabrication of the ISFET-based pCO$_2$ sensor is somewhat complicated: the process involves on-wafer deposition and lift-off of silver and subsequent chloridation of its surface,[9−12] prior to deposition of a hydrogel layer and a gas-permeable membrane.

Another drawback of the ISFET-based sensor devices concerns calibration drifts caused by their thermal sensitivity and photo-induced junction leakage currents.[13] One way to solve this problem is to use a differential measurement setup, i.e., an ISFET/REFET (reference FET) arrangement, as shown in Figure 1B. In the CO$_2$ sensing system, the REFET may be prepared by employing a buffered hydrogel layer inside the gas-permeable membrane. The concept of differential measurements comes from the fact that the two adjacent transistors on a single chip have virtually the same operational characteristics (i.e., the same drift, the same temperature coefficient, etc.). Therefore, calibration drifts of these two identical ISFETs cancel out, and the differential output signal comes from the pH change caused by diffused CO$_2$ in the pCO$_2$-FET side of the arrangement. It should be noted, however, that both the pCO$_2$-FET and the REFET need inner reference electrodes, again due to the high resistance of the gas-permeable membranes.

In this work, we describe a new type of differential pCO$_2$ sensor system that is much simpler in fabrication. The proposed device employs a low-resistance gas-permeable membrane for both the pCO$_2$-FET and the REFET in a differential arrangement (Figure 2). For example, a one-component RTV silicone rubber material containing an ion-complexing agent (e.g., valinomycin) is utilized as the gas-permeable membrane. In this configuration, while the pCO$_2$-FET is covered with a hydrogel-based recipient layer, as in the conventional case, the REFET is made without the layer, and

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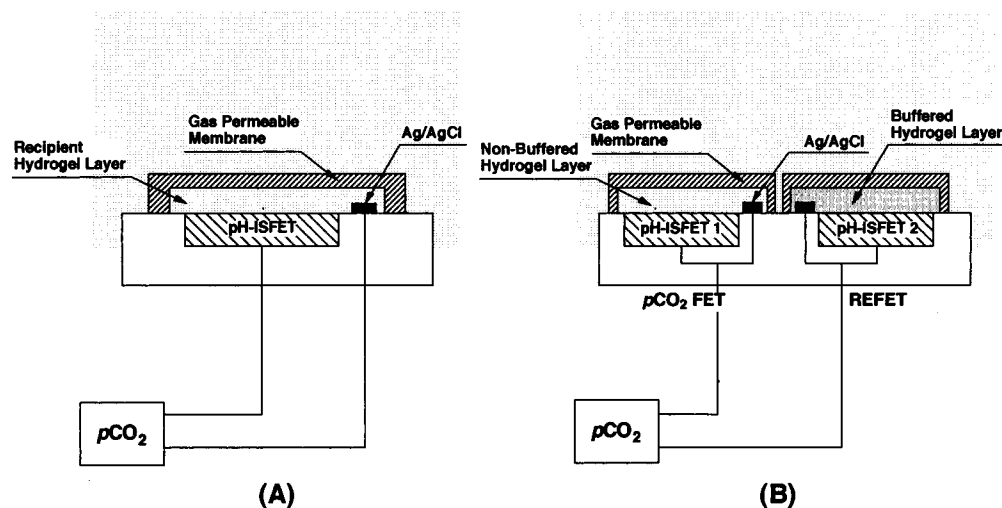(13) Goldberg, H. D. Ph.D. Thesis, University of Michigan, Ann Arbor, MI, 1993; Chapters II−V.

Figure 1. Schematic of the ISFET-based pCO_2 sensors: (A) Severinghaus type pCO_2 sensor and (B) Severinghaus-type differential pCO_2 sensor.
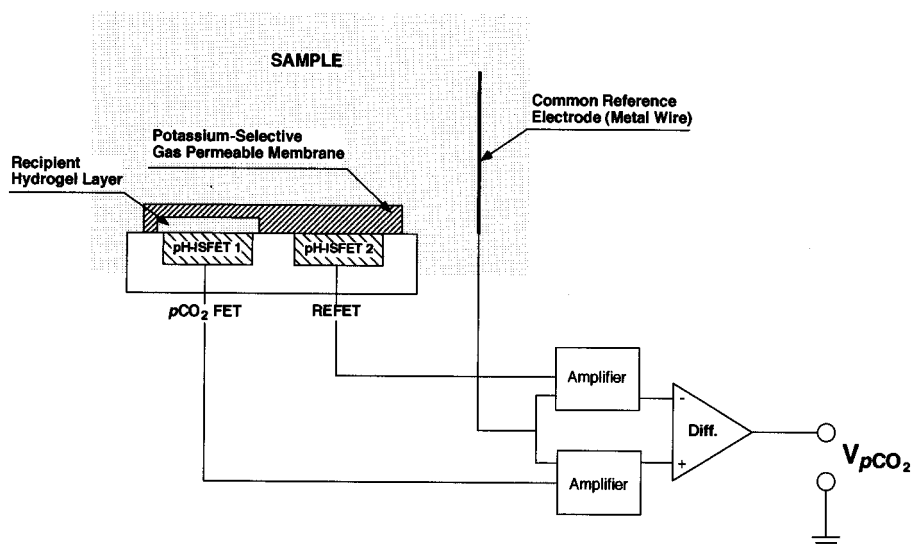

Figure 2. Differential CO_2 measurement setup employing a low-resistance gas-permeable membrane.

thus, there is no pH change by diffused CO_2. Since the resistance of the RTV membrane is substantially lowered due to the presence of the ion-complexing agent, the reference electrode can be placed outside the gas-permeable membrane (i.e., placed in the sample side) as a common reference for both FET's. Output signals from the pCO_2-FET and the REFET are measured against the common reference, and the difference of these two signals is measured through a differential amplifier; therefore, calibration drifts of the two identical ISFETs cancel out. The ion response, particularly potassium response, or the potential drifts caused by both parts of the membranes cancel out exactly the same way as in the case of the base ISFETs.

In the proposed sensor system, the common reference electrode is not required to exhibit a stable potential, because both signals from the pCO_2-FET and the REFET are measured simultaneously (i.e., the reference electrode functions merely as a zero point). Any metallic electrode (e.g., platinum, silver, etc.) can be used as the common reference and, thus, can be very easily incorporated into an integrated structure, simplifying the sensor fabrication. In this contribution, the factors affecting the response of the gas sensor (e.g., the composition of the gas-permeable membrane and hydrogel layer, etc.) and the characteristics of the

differential measurement setup (e.g., drift, temperature effect, residual ion response, etc.) are discussed.

EXPERIMENTAL SECTION

Reagents. Bis(2-ethylhexyl)adipate (DOA), bis(2-ethylhexyl) sebacate (DOS), bis(1-butylpentyl) adipate (BBPA), 2-nitrophenyl octyl ether (NPOE), potassium tetrakis(p-chlorophenyl)borate (KTpClPB), sodium ionophore III (ETH 2120), poly(acrylic acid), hydroxyethyl cellulose (medium viscosity 1), hydroxypropyl methyl cellulose, and poly(vinyl alcohol) (PVA; MW 22000 and 100 000) were purchased from Fluka (Ronkonkoma, NY). Valinomycin was obtained from Sigma (St. Louis, MO), diisodecyl adipate (DIDA) from Scientific Polymer Products, Inc. (Ontario, NY), and one-component silicone rubber (3140 RTV) from Dow Corning (Midland, MI). All other chemicals used were analytical-reagent grade. Standard solutions and buffers were prepared with deionized water.

Evaluation of Silicone Rubber Membranes. Various silicone rubber matrix membranes were prepared and tested for their pH response using conventional ion-selective electrodes as de-

scribed in our previous articles.[14,15] The membrane compositions tested were as follows: in addition to 3140 RTV, (a) 12 wt % DOA; (b) 12 wt % DOS; (c) 12 wt % NPOE; (d) 1.0 wt % KTpClPB; (e) 12 wt % DOS and 0.8 wt % valinomycin; and (f) 12 wt % DOA and 0.8 wt % ETH 2120. An aqueous solution of 0.1 M KCl was employed as the internal filling solution. The response of the membrane electrodes to pH changes was tested by adding aliquots of LiOH to a solution of 11.4 mM boric acid/6.7 mM citric acid/10.0 mM NaH_2PO_4 at room temperature.

Preparation of pCO_2 and Reference ISFETs. The ISFETs used in the present study were supplied by the Korea Electronics Co. Ltd. (Gumi, Korea) and were n-channel depletion mode FETs (each chip 0.6 mm × 1.2 mm). The gate insulator of the ISFET consisted of a 50 nm thick SiO_2 layer (formed by dry oxidation of Si) and a 50 nm thick Si_3N_4 layer (formed by low-pressure chemical vapor deposition). The pCO_2-FET was prepared by covering the gate surface with a hydrogel layer (10−20 μm thickness; 0.4−0.6 mm diameter) and a gas-permeable membrane (20−30 μm thickness; 1.0−1.2 mm diameter). The hydrogel layer was deposited by dispensing 2−5 μL of an aqueous mixture containing 4 wt % PVA, 5 mM $NaHCO_3$, and 0.5 mM NaCl, and by drying the film for 5 min. The gas-permeable membrane was formed by applying 15−20 μL of a mixture of 0.8 wt % valinomycin, 77.7 wt % silicone rubber, and 21.5 wt % plasticizer (DOA, DOS, etc.) dissolved in THF (200 μL for 100 mg of silicone rubber), evaporating the solvent, and curing the membrane overnight. In the case of the reference FET (REFET), the gate surface was covered directly with the gas-permeable membrane. Both the hydrogel layer and the gas-permeable membrane were cast with a 250 μL microsyringe (Hamilton, Reno, NV) under a microscope.

Evaluation of ISFET Response. The experimental arrangement for differential measurements is presented in Figure 2. The pCO_2-FET and REFET were connected through identical amplifiers to an IBM AT-type computer equipped with an analog-to-digital converter. The output signals, V_{Gas} and V_{Ref}, were measured against a common reference electrode (Orion Ag/AgCl; Model 90-02) in a constant drain−current mode ($I_d = 120$ μA) with a constant drain−source potential ($V_{ds} = 3$ V). A differential amplifier enabled the difference of these two signals ($V_{Diff} = V_{Gas} - V_{Ref}$) to be obtained. Response and calibration curves for CO_2 and K^+ were obtained from addition of standard solution ($NaHCO_3$ or KCl solution) to 200 mL of background electrolyte (0.2 M citrate−HCl, pH 4.5) at room temperature under stirring. In the case of the pH response, aliquots of NaOH were added to an electrolyte solution.

RESULTS AND DISCUSSION

It has been known that CO_2 as well as water vapor can permeate plasticized polymeric ion-selective membranes.[16−20] For example, Fogt et al.[16] demonstrated that potassium ISFETs employing valinomycin-doped PVC membranes are subject to positive interference by dissolved CO_2. On the other hand, Simon et al.[18,19] developed a differential CO_2 sensor system by taking advantage of the fact that CO_2 readily permeates pH-sensitive polymer membranes. Such a probe consists of two identical pH-sensitive membrane electrodes prepared by incorporating tridodecylamine as the H^+-selective ionophore in a plasticized PVC film. Both pH sensors employ internal reference electrodes (i.e., Ag/AgCl) and recipient solutions. In this differential scheme, the internal reference buffer of one of the pH sensors is a nonbuffered bicarbonate electrolyte (e.g., $NaHCO_3$/NaCl); the pH of this solution changes as a function of the sample pCO_2 and is detected by the inner sensing surface of the CO_2-permeable H^+-selective PVC membrane. The second pH electrode has a strong buffer as its internal recipient solution, and thus the pH of this second inner solution does not change as a function of the sample pCO_2. Since both pH sensors use identical H^+-selective membranes, the sample pH cancels at equilibrium in this differential mode (see refs 16−18 for a more detailed description).

However, such a pH sensitivity of the gas-permeable polymer membrane (i.e., the aforementioned tridecylamine-doped PVC membrane) is not acceptable to our new ISFET-based differential CO_2 sensor scheme: if the membrane is pH-responsive, the pH change, caused by diffused CO_2, will be detected not only by the pH-sensitive surface of the ISFET (i.e., pH-ISFET 1 in Figure 1 in Figure 2) but also by the inner side of the gas-permeable membrane simultaneously. Since these responses are in opposite directions, the detected CO_2 signals cancel out. Therefore, for a desired performance of the proposed sensor system, it is critical that the low-resistance gas-permeable membrane must exhibit a negligible response to the pH change.

Another problem associated with the use of PVC-based membranes in ISFET-based sensor devices is inherently weak adhesion of PVC matrices to the gate oxide of an ISFET chip.[13,21−23] This adhesion problem becomes more serious when the sensor employs a recipient electrolyte layer between the outer membrane and the ISFET gate oxide. Osmotic transport of water into this electrolyte layer can further accelerate detachment of the polymer membrane from the gate of the ISFET device that renders the sensor inoperative.

One-part room temperature vulcanizing (RTV) silicone rubber has received attention as a possible alternative to PVC for fabricating solid-state type ion sensors, because it exhibits high bond strength to a wide range of substrates.[2,13−15,23−25] Very recently, we have described new carbonate[14] and calcium[15] ion-selective membranes employing highly plasticized RTV silicone rubber matrices. These membranes were shown to exhibit enhanced performance, in terms of petentiometric response and selectivity, compared to the corresponding PVC-based membranes. We[14,15] also demonstrated that addition of plasticizer to the silicone rubber matrix does not significantly deteriorate its adhesive property, and even a highly plasticized RTV membrane

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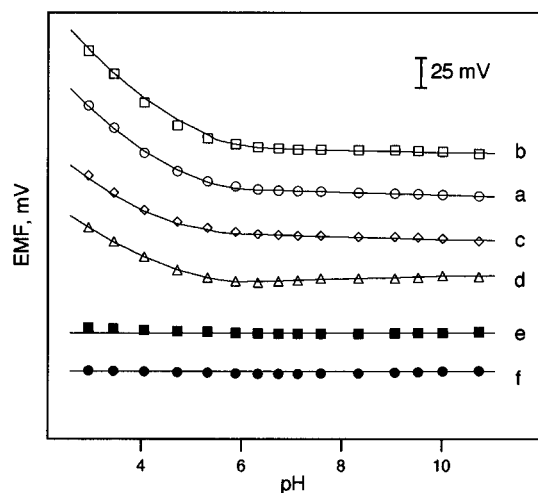
Figure 3. pH response of silicone rubber matrix membranes employing different active components: (a) DOA, (b) DOS, (c) NPOE, (d) KTpClPB, (e) DOS/valinomycin, and (f) DOA/ETH 2120. The membranes were tested in conventional electrode bodies.

Figure 4. pH response of the pH-ISFET coated with a valinomycin-doped RTV silicone rubber film.

retains adhesion much more strongly than the PVC membrane. A highly adhesive property of the membrane is particularly important in our ISFET-based differential sensor system: this not only ensures the longer sensor lifetime but also prevents the formation of an aqueous layer between the membrane and the pH-sensing surface of the ISFET at the REFET side (i.e., pH-ISFET 2 in Figure 2).

The high electrical resistance of RTV silicone rubber membranes can be lowered by incorporating lipophilic ionic additives or plasticizers to the matrices. However, these membranes do exhibit significant response to pH changes particularly in the range of acidic pH, as tested in conventional electrode bodies [see curves a (DOA), b (DOS), c (NPOE), and d (KTpClPB) in Figure 3]. This is probably due to the presence of ionic sites (e.g., silanol groups or ionizable impurities) within the RTV silicone rubber membrane phase. As stated, such pH-responsive membranes are not desired for use as a low-resistance gas-permeable membrane in our ISFET-based gas sensor configuration. However, the pH response of the plasticized silicone rubber membranes disappeared when the membranes were doped with neutral carrier-type cation ionophores [see curves e (K^+/valinomycin) and f (Na^+/ETH 2120) in Figure 3]. It is assumed that the neutral carrier-mediated selectivity overrides the intrinsic pH response of the silanol-terminated silicone rubber matrix membranes. It has been our experience that the valinomycin-doped membranes usually exhibit better stability and lifetime than those doped with other ionophore systems, and that potassium-selective ISFETs employing the valinomycin-based silicone rubber membranes function even after 9 months of use. Thus, we selected the valinomycin-based potassium-selective membrane system as a low-resistance gas-permeable membrane for use in the present pCO_2 sensor device.

Prior to fabricating pCO_2 sensors, the base ISFETs were tested for their pH response by employing a conventional ISFET measurement setup, and all pH-ISFETs employed in this study displayed appropriate pH response, with a slope of 55−59 mV per unit pH change. As a preliminary experiment, the gate area of a pH-ISFET was coated with a valinomycin-doped silicone rubber membrane (0.8 wt % valinomycin, 77.7 wt % silicone rubber, and 21.5 wt % DOA). As can be seen in Figure 4, the resulting
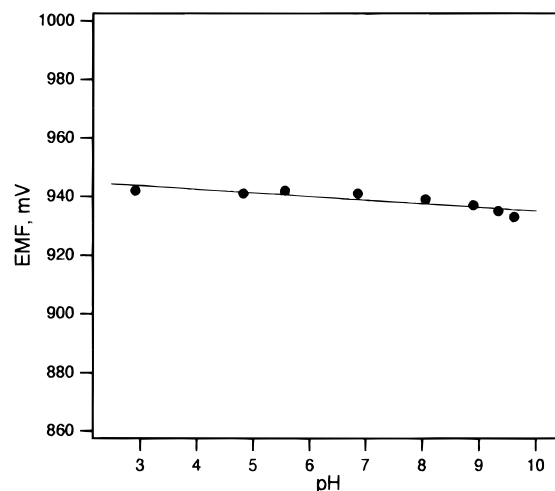
potassium sensor indeed exhibited a negligible response to pH, with a slope of less than 1 mV per unit pH change.

For CO_2 response of the gas FET, several steps are involved: the CO_2 diffusion from the sample to the hydrogel layer; the equilibrium reaction generating hydrogen ions; and the diffusion of hydrogen ion or CO_2 species to the ISFET surface through the hydrogel layer. Therefore, both the gas-permeable membrane and the hydrogel layer compositions need to be optimized for a desirable CO_2 sensor response. For the recipient hydrogel layer, we have tested the following hydrophilic polymeric materials: poly(vinyl alcohol) (PVA; MW 10 000, 22 000, 40 000, and 100 000), poly(acrylic acid) (MW 2100, 20 000, and 170 000), hydroxyethyl cellulose, and hydroxypropyl methyl cellulose. In this experiment, an aqueous mixture containing 4 wt % polymer, 5 mM $NaHCO_3$, and 0.5 mM NaCl was applied to form a hydrogel layer on the gate surface prior to casting a gas-permeable membrane. Poly-(acrylic acid) resulted in sensors with negligible CO_2 response, probably because this acidic polymer lowers the pH of the recipient solution and acts as a buffer with $NaHCO_3$. The use of cellulose-based materials was abandoned because they become rigid upon lowering the solution temperature. Sensors prepared with a high molecular weight PVA (e.g., 40 000 and 100 000) exhibited a slow and reduced CO_2 response compared to those prepared with a low molecular weight PVA (e.g., 10 000 and 22 000). We also examined the effects of the PVA content or the $NaHCO_3$ concentration of the casting mixture on the resulting sensor performance. Briefly, the CO_2 response of the sensor was slower when the weight percentage of PVA was greater than 4 wt %. Three different concentrations of $NaHCO_3$ were tested: the sensor response was slower with 25 mM $NaHCO_3$ and was less with 0.5 mM $NaHCO_3$ than that prepared with 5 mM $NaHCO_3$. For the subsequent study, we selected the following composition to form a recipient hydrogel layer: 4 wt % PVA (MW 22 000), 5 mM $NaHCO_3$, and 0.5 mM NaCl.

The valinomycin-based gas-permeable membrane has been optimized by varying the amount and type of plasticizer incorporated in the silicone rubber matrix membrane. The sensor signal was somewhat unstable, with the membrane containing less than 10 wt % plasticizer. However, the sensor employing more than 25 wt % plasticizer exhibited a reduced CO_2 response without further improving the signal stability. In Table 1, effects of changing the type of plasticizer on the response properties of the

Table 1. Response Characteristics of the pCO₂ Sensors Coated with Silicone Rubber Membranes Employing Different Plasticizers[a]

plasticizer[b]	response time $t_{95\%}$, s[c]	recovery time t_{rec}, min[d]	slope mV/decade[e]
DOA	105	19.0	40.6
DOS	99	18.9	41.5
DIDA	153	>30	39.6
NPOE	246	>30	49.6
BBPA	249	>30	58.6

[a] Hydrogel layer composition: 4 wt % poly(vinyl alcohol), 5 mM NaHCO₃, and 0.5 mM NaCl in water. Membrane composition: 77.7 wt % silicone rubber, 0.8 wt % valinomycin, and 21.5 wt % plasticizer. [b] DOA, bis(2-ethylhexyl) adipate; DOS, bis(2-ethylhexyl) sebacate; DIDA, diisodecyl adipate; NPOE, 2-nitrophenyl octyl ether; BBPA, bis(1-butylpentyl) adipate. [c] From background to 1.64 mM CO₂. [d] From 1.64 mM CO₂ to background. [e] Range, 0.82−4.15 mM.

resulting CO₂ sensors are summarized, in terms of response time ($t_{95\%}$, the time required to reach 95% of the equilibrium potential), recovery time (t_{rec}, the time required to reach 95% of the background potential), and response slope in the range of clinical interest. In this experiment, the gas-permeable membranes were prepared employing the same amount of plasticizer (i.e., 21.5 wt %) and valinomycin (0.8 wt %), and the conventional ISFET measurement setup was employed with the reference electrode placed outside the gas-permeable membrane. As can be seen, the sensors employing DOA and DOS exhibited much faster response properties than those with DIDA, NPOE, and BBPA as the plasticizer. On the other hand, the CO₂ response slope was greater with the sensors with NPOE and BBPA. In this report, we present the dynamic response of the sensors employing two different plasticizers, i.e., DOA for a faster response or recovery time with a lower slope (Figure 5A) and BBPA for a greater slope with a slower response (Figure 5B). For both sensors, the calibration curves were found to be linear in the clinical range of dissolved CO₂ (i.e., 1−3 mM) for human blood: 40.6 mV/decade with DOA and 58.6 mV/decade with BBPA. We selected DOA, which gives the faster response properties, and employed the following composition as the gas-permeable membrane for the substituent experiments: 0.8 wt % valinomycin, 21.5 wt % DOA, and 77.7 wt % silicone rubber.

With the selected compositions of the gas-permeable membrane and the recipient hydrogel layer, we prepared the pCO₂ and reference ISFETs and further examined the sensor characteristics. First, the potential drifts for newly prepared sensors from dry to wet (in the first 2 h) were evaluated by monitoring the sensors continuously in the background electrolyte (0.2 M citrate−HCl, pH 4.5), as shown in Figure 6. For the pCO₂-FET (curve a), a large potential jump was observed during the initial 10 min period due to osmotic transport of water into the hydrogel layer (see curve a in Figure 6). On the other hand, the REFET (curve b), in which the gate oxide is coated with the same valinomycin-based silicone rubber membrane, but without the hydrogel layer, exhibited no significant initial signal drift. This can be explained by a strongly adhesive property of the silicone rubber membrane to the silicon nitride, which minimizes the formation of an aqueous layer between the membrane and the pH-sensing surface of the ISFET. Once the osmolarity between the internal electrolyte and the sample solution reaches an equilibrium, the sensors exhibit a stable potential, and even additions of high levels of NaCl (10−
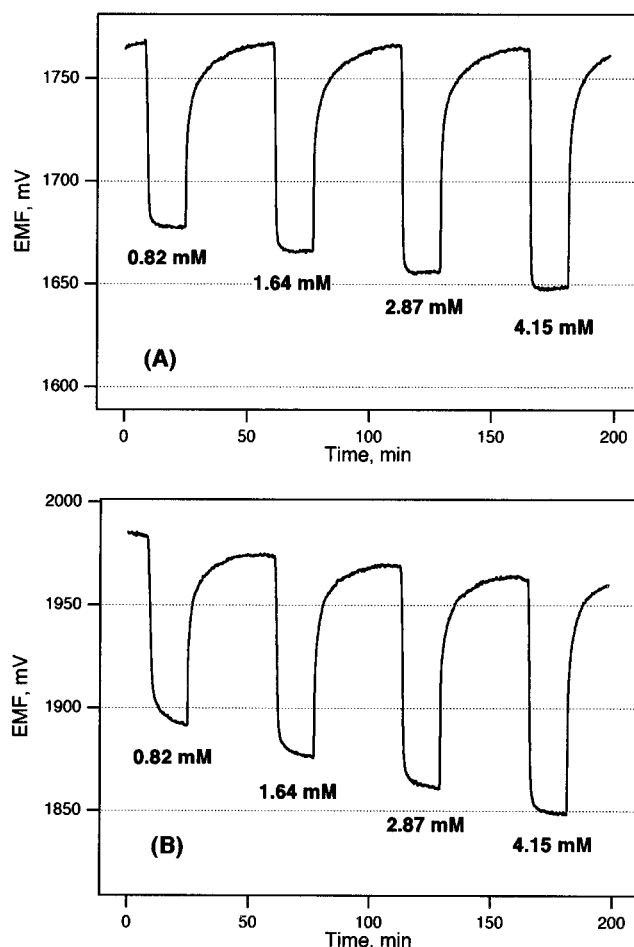

Figure 5. Dynamic response of the pCO₂ sensor prepared with valinomycin-doped silicone rubber incorporating (A) bis(2-ethylhexyl) adipate and (B) bis(1-butylpentyl) adipate.
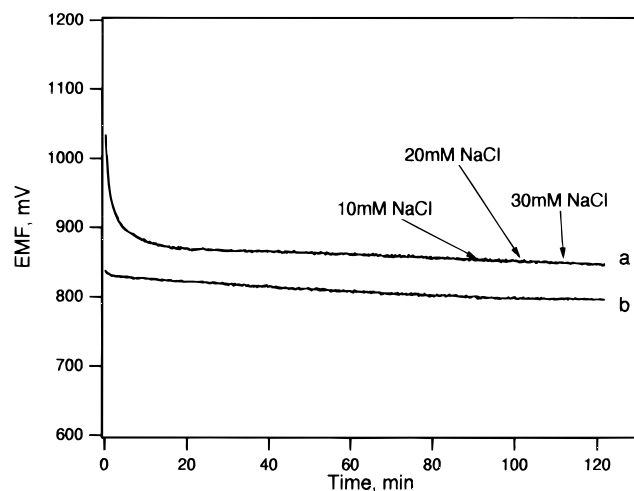

Figure 6. Potential drifts of newly prepared (a) pCO₂-FET and (b) REFET after immersing the sensors in an aqueous solution (0.2 M citrate−HCl, pH 4.5).

30 mM) to the background electrolyte do not influence the sensor signal, as demonstrated in Figure 6.

These pCO₂-FET and REFET systems were employed in the three-electrode-based differential measurement system depicted in Figure 2. In this preliminary experiment, a conventional Ag/AgCl reference electrode was used as the common reference. Figure 7 illustrates the sensor response to added potassium. As can be seen, the individual responses of the pCO₂ FET (curve a)
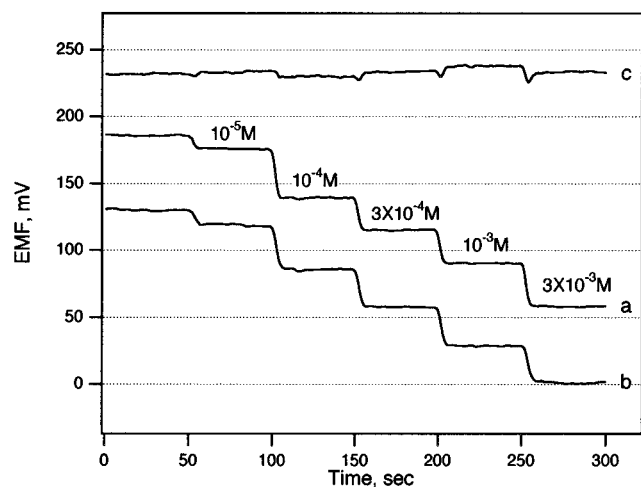
Figure 7. Potassium response of the individual (a) pCO_2-FET and (b) REFET and of (c) the differential pCO_2 measurement setup.
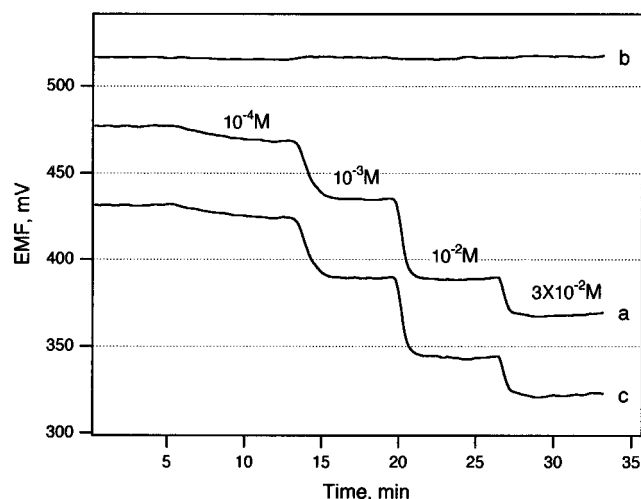

Figure 8. CO_2 response of the individual (a) pCO_2-FET and (b) REFET and of (c) the differential pCO_2 measurement setup.

Figure 9. Effect of the temperature change on the output signal of the individual (a) pCO_2-FET and (b) REFET and of (c) the differential pCO_2 measurement setup.

and the REFET (curve b) are virtually the same, demonstrating that both membranes on the gas FET and the REFET possess the same response properties. Indeed, the differential system (curve c) canceled these signals and did not exhibit the response toward added potassium. It is believed that errors caused by other types of membrane signals (e.g., potential drifts, interfering response to ions other than K^+, asymmetry potentials caused by protein adsorption, etc.) can be corrected by the proposed differential arrangement.

In Figure 8, the CO_2 response of the sensor system was examined by adding aliquots of $NaHCO_3$ to generate the appropriate levels of dissolved CO_2 in the background electrolyte. Previously, Fogt et al.[16] reported that the potassium ISFETs coated with valinomycin-doped PVC membranes displayed a large response toward CO_2 due to the presence of a hydrated layer formed between the gate and the PVC membrane. However, the REFET, prepared in the present study by coating the ISFET with the valinomycin-doped silicone rubber membrane, showed no response to dissolved CO_2 (curve b in Figure 8). We confirmed that this sensor did not exhibit any observable response toward CO_2 generated in a solution containing 0.1 M $NaHCO_3$, even after a week of use. From this fact, it is obvious that the adhesion of the potassium-selective silicone rubber membrane is strong enough to prevent the forma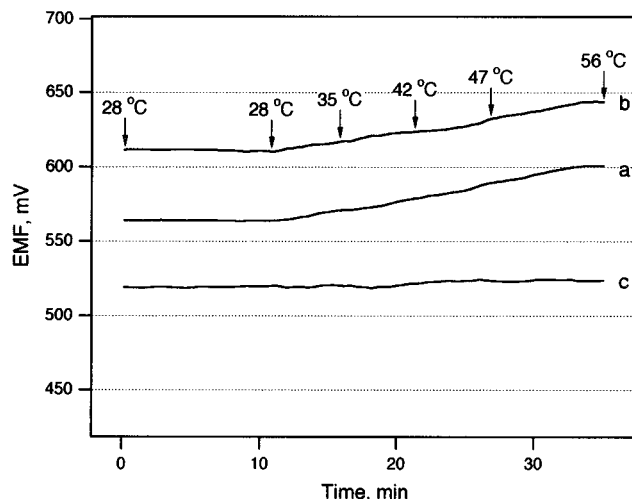tion of an aqueous layer between the membrane and the gate surface of the ISFET. On the other hand, the pCO_2-FET displayed the expected response to dissolved CO_2, and, therefore, the response of the differential system (curve c in Figure 8) is identical to the response of the pCO_2-FET (curve a). The differential sensor system yielded a slope of 41 mV/decade in the range of 0.1–30 mM total CO_2, with a lower detection limit of 0.03 mM and a upper limit of 30 mM, and functioned well after a week of use.

Finally, we examined whether the proposed differential system overcome calibration drifts, for instance, those caused by the temperature change. As can be seen in Figure 9, as the temperature increased in the sample solution, both FETs exhibited significant signal drifts (curves and b), but to the same extent in the same direction. As expected, the differential system was not subject to such signal drifts, because these identical drifts cancel in the differential measurement mode (curve c). This experiment indicated that the intrinsic drift[16] of the ISFET-based sensors can also go undetected by this unique differential measurement arrangement.

In this report, a new approach of fabricating the ISFET-based differential CO_2 sensor device has been described by using the low-resistance ion-selective gas-permeable membrane. Since the emphasis is on implementing the proposed concept in the present study, the differential sensor system was not evaluated after a week of use. In recent years, however, various types of disposable sensors have been applied successfully in commercial clinical laboratory instruments: a module ($pH/pO_2/pCO_2$) for 15 or 30 samples (StatPal, SenDx Medical, Inc., La Jolla, CA) and a cartridge ($Na^+/K^+/Cl^-$) for 2 days of use or 400 samples (Dimension AR, Du Pont Diagnostics, Wilmington, DE), as well as cartridges for a single use (i-STAT, i-STAT Corp., Princeton, NJ), for 2 weeks of use (GEM Premier, Mallinckrodt Sensor Systems, Ann Arbor, MI), etc. The fabrication of the sensor device presented in this report is compatible with the semiconductor process, if the screen-printing technology is employed for depositing the silicone rubber membranes.[13] Since the process for making the reference electrode on top of the ISFET sensors is not needed, it is likely that the proposed approach will offer a relatively simple method to mass-fabricate the pCO_2 sensor devices.