A Small pH Sensor Catheter of the Endoscope for Acidity Test of Gullet and Stomach

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The detection of pH in the gullet and stomach is highly significant for the diagnosis of gastroesophageal reflux disease (GERD), particularly with the use of a pH sensor in vivo. Most conventional pH sensors are used singly and could not be inserted in the endoscope’s working channel. Because the ion sensitivity field-effect transistor (ISFET) chip has become very small, we have made the pH sensor smaller than a conventional glass pH sensor, and have used it. In this paper, we introduce a small in vivo pH sensor catheter of 2.7 mm diameter and 8 mm length, which can be put in the endoscopy’s working channel of 3 mm diameter. The catheter was evaluated in buffer solution (pH 2–12) and its sensitivity was 43 mV/pH. It was confirmed that the catheter properly functioned during an animal experiment.

1. Introduction

With the advance of semiconductor sensor technology, DNA chips, lap-on-a-chip sensors, protein sensors and other similar devices have been used in medical diagnosis. There are few sensors that can probe the gastrointestinal (GI) tract. However, such sensors have limits in diagnosing stomach disorder. Physicians of digestive diseases have raised the need for a pH sensor catheter for the diagnosis of ulcers, tissue inflammation, hypo- or hyper- chlorhydria, achlorhydria, and esophageal acid exposure. Some wireless pH sensors have been developed recently, and physicians want to use a pH catheter during an endoscope test.\(^1\-3\)

The pH of the gullet and stomach is significant and useful for the diagnosis of GERD, particularly for functional diseases of GERD. Most conventional pH sensors are too large to put into an endoscope’s working channel. Because an ion-sensitive field effect
transistor (ISFET) pH sensor is smaller than a normal glass electrode pH sensor, it can be inserted and used as a pH sensor catheter in an endoscope working channel. However, it is difficult to make the reference electrode smaller and to maintain the performance as good as that of the large conventional one.

In this paper, we discuss the fabrication of an ISFET pH sensor catheter for insertion into an endoscope working channel and investigated the digestive organ.

2. Structure and Fabrication

2.1 Structure of the ISFET pH sensor catheter

An ISFET is a potentiometric pH sensor that is easily adapted to a wide range of chemical, biochemical, and biomedical measurements. Because an ISFET pH sensor is smaller than a conventional glass electrode pH sensor, it can be used to determine pH in the endoscope working channel. Figure 1 shows a schematic of the use of our ISFET pH sensor catheter.(4,5)

We designed, implemented, and evaluated a small ISFET pH sensor for insertion into an endoscope working channel. The pH sensor catheter is composed of an ISFET on a printed circuit board (PCB), a reference electrode, and electrical wires. The PCB width was limited to within 2.5 mm because the diameter of the endoscope working channel was 3 mm. The reference electrode was fabricated using Ag/AgCl wire (0.5 mm diameter), KCl gel, and ion-exchangeable glass. The pH sensor catheter had a cap. It was made of polyetherimide (PEI), and was 2.7 mm in diameter and 8 mm in length.

The pH of an aqueous solution indicates the molar concentration of hydrogen ions. As with the schematics of other semiconductor ion sensors, the ISFET schematic is similar to that of a metal insulator semiconductor field-effect transistor (MISFET). The gate part of a MISFET is replaced with a reference electrode and becomes an ISFET

![Fig. 1. Overall view of an ISFET pH sensor catheter in the endoscope.](image)
sensor with solution and ion sensitivity membranes. The reference electrode keeps the potential in the solution. Hydrogen ions in the solution react with silicon nitride on the sensing membrane, and an electrochemical potential difference is generated between the reference electrode and the sensing membrane. The potential difference is a function of ion concentration; it changes the channel conductivity between the source and drain of ISFET. Thus, the drain current was altered linearly to the pH. Figure 2 shows a schematic of an ISFET.\(^4\)

2.2 Fabrication

The size of the pH sensor was determined using the reference electrode because the small size of the ISFET is dependent on the size of the reference electrode. The miniaturization of the reference electrode is required to make the pH sensor acceptably small. Over the years, many research studies of quasi-metal electrodes and novel metals such as Au and Pt have been conducted. These studies showed that the pH sensor cannot be realized owing to the instability of the metal surface potential and extreme drift. Therefore, we developed a pH sensor catheter that has a very small reference tube, that is, a Ag/AgCl electrode. To miniaturize the reference electrode, the quantity of KCl, the reaction length of Ag/AgCl, and the aperture size of the ion exchange membrane were optimized through a number of experiments. Figure 3 shows a schematic of the ISFET pH sensor catheter.
pH sensor head. The cap is divided into two parts. The ISFET chip is on the upper side and the reference Ag/AgCl electrode kept in KCl gel is on the lower side.

The pH sensor catheter was packaged with silicon epoxy to protect it against strong acids and alkalis and to eliminate the leakage current of the ISFET. Silicon epoxy is thermostable, inactive, nonadhesive, insulated, and resistant to acids and alkalis.

The pH sensor catheter of 2.7 mm diameter and 8 mm length was fabricated for appropriate use in an endoscope’s working channel of 3 mm diameter, as shown in Fig. 4. The reading circuit was a reference feedback circuit. This circuit keeps the drain current of the ISFET stable, and the voltage of the reference electrode increases with increasing pH. (5–9)

3. Results and Discussion

3.1 Sensitivity

The most important property of the pH sensor catheter is reliability. Therefore, we carried out an experiment to compare our proposed electrode with a large reference electrode to confirm whether a small electrode will operate well. The large reference electrode was 4.5 mm in diameter and 7 cm in length, and the small one was 2.7 mm in diameter and 8 mm in length. We measured the $I_d-V_d$ and $I_d-V_g$ curve characteristics of the pH sensor with the large reference electrode using a semiconductor analyzer. Figure 5 shows the $I_d-V_d$ and $I_d-V_g$ curves of the pH sensor using the large reference electrode. The current difference at each pH increased linearly.

The pH sensor with the small reference electrode was also examined. Figure 6 shows that the $I_d-V_d$ and $I_d-V_g$ curves of the pH sensor using the small reference electrode are similar to those shown in Fig. 5. We confirmed that both electrodes have linearity in standard buffer pH solutions, as shown in Figs. 7 and 8. As the size of either electrode was reduced, the $I_d$ current decreased from 149 µA to approximately 49 µA. Thus, the sensitivity was decreased slightly but the output level increases orderly similarly to pH.

![Fig. 4. Fabricated ISFET pH sensor catheter.](image-url)
Fig. 5. $I_d-V_d$ and $I_d-V_g$ characteristics of large reference electrode.

Fig. 6. $I_d-V_d$ and $I_d-V_g$ characteristics of small reference electrode.
This work showed that it is possible to use the small reference electrode with an ISFET pH sensor.

The sensitivity of the pH sensor catheter was measured from pHs 2 to 9 with the reference feedback circuit. It was dipped in each pH buffer solution for 1 min. The sensitivity was 43 mV/pH from pHs 2 to 9. The test was repeated four times, in both increasing and decreasing orders. The pH of the stomach and gullet is between 2 and 7, and this sensor can be useful for the human body. Figure 9 shows the sensitivity of the pH sensor catheter.

### 3.2 Long-term stability test

The long-term stability test is essentially to confirm the reliability of the sensor. The catheter will be used in the stomach and gullet within 2 or 3 h at most. The pH sensor catheter was soaked in pH 2 or 7 solution for 72 h. The solution at 37°C was stirred with a magnetic bar. Figure 10 shows the long-term stability test results of the pH sensor catheter.

### 3.3 In vivo animal test

An in vivo test on the fabricated pH sensor catheter was carried out in a pig. The test was conducted with an endoscope, so we could determine where the catheter was. The pH sensor catheter worked well in the gullet and stomach of the pig. When the catheter reached the stomach, the pH dropped rapidly. Figure 11 shows that the catheter could determine the pH of a pig’s alimentary canal.
Fig. 9. Sensitivity of small pH sensor catheter of endoscope.

Fig. 10. Long-term stabilities at pHs 2 and 7.

Fig. 11. pHs of gullet and stomach of animal.
4. Conclusions

In this study, we developed a small pH sensor catheter that could be inserted into an endoscope's working channel of 3 mm diameter using ISFET and the microreference electrode filled with KCl gel. The packaging materials were chosen to be suitable for contact with the human body. The sensitivity of the pH sensor catheter was 43 mV/pH. Its durability was tested at pHs 2 and 7 for 72 h, and the results showed that it worked well. In an animal, it was successfully used to determine pH.

The sensor has potential for commercialization. When the endoscope showed the gullet and stomach, it was found that the catheter can be used to examine those regions as well. The results could be obtained in real time, thus more accurate diagnoses are expected.

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