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Encapsulation of Gas Sensors to Operate in the Gastrointestinal Tract for Continuous Monitoring

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Abstract

Recent advances in ingestible sensors have enabled in situ detection of gastrointestinal (GI) biomarkers which shows great potential in shifting the paradigm of diagnosing GI and systemic diseases. However, the humid, acidic gastric environment is extremely harsh to electrically powered sensors, which limits their capacity for long term, continuous monitoring. Here, we propose an encapsulation approach for a gas sensor integrated into a nasogastric (NG) tube that overcomes chemical corrosion, electrical short, and mechanical collision in a gastric environment to enable continuous gaseous biomarkers monitoring. The coating effects on the sensitivity, signal latency, and repeatability are investigated. Our long-term continuous monitoring in vitro results show that the proposed coating method enables the gas sensors to function reliably and consistently in the simulated GI environment for more than 1 week. The encapsulation is composed of Polycaprolactone (PCL) to protect against mechanical scratching and Parylene C to prevent a sensor from chemical corrosion and electrical short. The average life-time of the sensor with 10 micrometers Parylene coating is about 3.6 days. Increasing the coating thickness to 20 micrometers results in 10.0 days. In terms of repeatability, 10 micrometers and 20 micrometers Parylene C coated sensors have a standard deviation of 1.30% and 2.10% for its within sensor response, and 5.19% and 3.06% between sensors respectively.

Keywords

gas sensor; encapsulation; gastrointestinal tract; continuous biomarkers monitoring

I. Introduction

The gastrointestinal (GI) tract provides several opportunities for non-invasive diagnosis and therapy. It contains a large amount of disease relevant biomarkers and has close proximity to internal organs for measuring physiological signals [1], [2]. Additionally, sensors can be

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easily introduced to the gastrointestinal tract without the use of surgical techniques. Recent advances in the development of ingestible sensors have demonstrated the possibility of in situ detection of various gaseous molecules [3], pressure [4], pH [5], temperature [6], and GI motility [7].

Steiger et al. have revealed that more than 90% of biomarkers detectable in blood can be found in gastric fluid [8]. They also showed that it is possible to detect ketone bodies in a swine stomach using a gas sensor that is integrated into the tip of a nasogastric (NG) tube immediately after intravenous administration of acetone. More recently, Huang et al. demonstrated detection of the inflammatory biomarker nitric oxide (NO), directly at the inflammatory site in an artificially induced colitis model in a swine via an ingestible electrochemical gas sensor [9]. These discoveries open the window to in situ diagnoses of GI diseases using ingestible sensors.

The gastrointestinal environment is highly humid and acidic, which is extremely harsh to electronics. To effectively sense gaseous biomarkers in the GI tract, gas sensors must be exposed to the environment to permit inflow of molecules, while preventing corrosion from fluids. A variety of research efforts have been dedicated to developing membranes that are selective permeable [3], [10]. However, there are no reported encapsulation solutions that can maintain a sensor's performance for a prolonged period, hence limiting the capacity for continuous monitoring.

In this paper, we propose a conformal coating strategy that utilizes both Polycaprolactone (PCL) and Parylene C to provide the sensor with protection against chemical corrosion, electrical short circuit and mechanical collision. PCL and Parylene C with varying coating thicknesses were applied onto two off-the-shelf sensors measuring gaseous molecules, temperature and humidity to investigate the effect of coating thickness on the sensor's long-term performance in terms of latency, sensitivity, repeatability, and sensor lifetime.

II. Materials and Methods

A. Sensor Encapsulation

Parylene C can form a very dense polymer network that would greatly reduce the water vapor permeability, thus preventing sensors from electrical shorting and chemical corrosion in the gastric environment. However, the conformal Parylene C coating is brittle and sensitive to mechanical deformation. Here, we utilize the high elasticity of PCL to enable the mechanical protection of Parylene C coated sensor.

A volatile organic compound (VOC) sensor (SGP40, Sensirion) and a temperature-humidity sensor (BME688, Bosch) were first coated with Parylene C with a coating thickness of 10 μm and 20 μm by means of the SCS Labcoter® 2 Parylene Deposition System [11]. Similar to solvent casting techniques used to create thin films [12], we used a solution that is made by dissolving 1 gram of PCL (M_n=50000) in 1 dL of dichloromethane (DCM) to create a conformal layer via dip coating on the Parylene C coated sensors. The evaporation of DCM would solidify the PCL coating and result in a highly porous structure, which

endows the PCL coating with good gas permeability. The overall PCL coating thickness is approximately 100 μm and was reached after two dipping cycles.

Using a scanning electron microscope (SEM) it is observed that the PCL has a mean pore diameter of 2.983 μm with standard deviation of 2.237 μm in flat areas.

B. Data Acquisition

We sampled the environment including the humidity, temperature, and the gaseous molecules, every five seconds using the SGP40 and BME688. The BME688 is capable of outputting temperature, humidity, pressure and gas readings, while the SGP40 is solely a VOC gas sensor. The sensors communicate with an Adafruit Feather M0 microcontroller (MCU) through an I^2C multiplexer (MUX). The MUX enables us to connect up to eight sensors with identical I^2C addresses.

C. In Vitro Setup Emulating Gastric Environment

In order to emulate the gastric environment, the sensors were kept in simulated gastric fluid at 37 degrees Celsius throughout the experiment. Every 12 hours, the sensors were exposed to a VOC, which is a 6.67% ethanol solution, for 30 minutes. Subsequently, the solution was refreshed to resemble the gastric emptying frequency.

The digital raw VOC value of the SGP40 and the temperature and humidity of BME688 are monitored throughout the experiment. Meanwhile, the pumps that control the inflow of simulated gastric fluid, VOC solution and outflow of fluid are controlled by the same main station that receives the sensor data. A detailed view of the simulated gastric environment is schematically shown in Fig. 3.

D. Evaluation Criteria

SGP40 sensors were evaluated on their sensitivity and the latency of the VOC response signal with different coating thickness. We define the sensitivity of the sensor to be the digital raw sensor value after 30 minutes of exposure to the VOC solution, which is right before the VOC solution in the simulated gastic environment is emptied. The latency of the SGP40 signal is determined by the time where the rate of change of the VOC signal is maximum. The sensors are considered at the end of its lifetime when the repeated sensitivity shows a deviation more than 10%, or an electrical short circuit caused the sensor breakout board to fail completely.

III. Results and Discussion

A. PCL Coating Effect on the Sensor Dynamic Response

It is important to note that any additional coating would inevitably change the sensor performance in terms of dynamic response and sensitivity. Fig. 4. shows the dynamic response of the SGP40 with and without the PCL coating exposed to a VOC in the air.

The PCL coated sensor has less noise than the uncoated sensor, whereas its difference in sensitivity and latency is negligible. Both sensors responded to VOC and reached the

steady state almost immediately. This result shows the porous PCL coating has good VOC permeability. However, it is also shown that it took much longer for the PCL coated sensor to recover to its original value. The delay of recovery might be caused by the residual VOC in the sensor's intrinsic membrane and the porous PCL.

B. Parylene C Coating Effect on the Sensor Dynamic Response

Parylene C is known for low gas permeability due to its dense polymer network. Fig. 5 shows the dynamic response to VOC solution of the sensors coated with 10 μm and 20 μm Parylene C via two different experiments. The 10 μm coated SGP40 shows a stronger sensitivity to the VOC solution when looking at the equilibrium value of the signal. The fluctuation of temperature was mainly caused by the simulated gastric emptying using room temperature simulated gastric fluid. It is shown that the 20 μm Parylene coated sensor is more sensitive to the thermal noise than the 10 μm coated counterpart because the reduction in sensitivity decreases the signal to noise ratio.

Notably, our results show the proposed encapsulation method increases VOC sensing precision in the simulated gastric environment (Table I). The variations in the repeatability of both the 10 μm and 20 μm coating within and between the sensors are all below 6%.

C. Encapsulation Effects on Long-term Sensor Performance

Although the coating attenuates the gas sensor's dynamic response, it significantly prolongs the sensor's lifetime to operate in a harsh environment. Fig. 6(a) shows the SGP40 with a 20 μm coating survives on average 10.0 days, whereas its 10 μm coated counterpart only survives for 3.7 days on average. The difference is even more apparent for the BME688 of which the average lifetime with 20 μm Parylene C coating is ten times higher than a BME688 sensor with a 10 μm coating.

Finally, we perform a statistical analysis of the coating thickness effect of the signal latency of the SGP40 as shown in Fig. 6(b). The VOC signal reaches its maximum rate of change after 7.9 minutes at a coating thickness of 20 μm, whereas it reaches this within 1 minute for 10 μm. This indicates a large change in diffusion speed for both coatings.

IV. Conclusion

This paper proposes an encapsulation method for a gas sensor integrated on an NG tube to continuously operate in the GI tract. In this work, we elucidate the coating effects on the gas sensor's dynamic response to VOCs, sensitivity, repeatability, latency and lifetime in a simulated gastric environment. Our results demonstrate that the synthesized porous PCL coating does not influence the gas sensor's sensitivity in air and reduces noise. Experiments with 10 μm and 20 μm Parylene C coatings show there is a strong trade-off between the sensor's lifetime and sensitivity. We also demonstrate that the encapsulation increases sensing precision in a simulated gastric environment.

Acknowledgments

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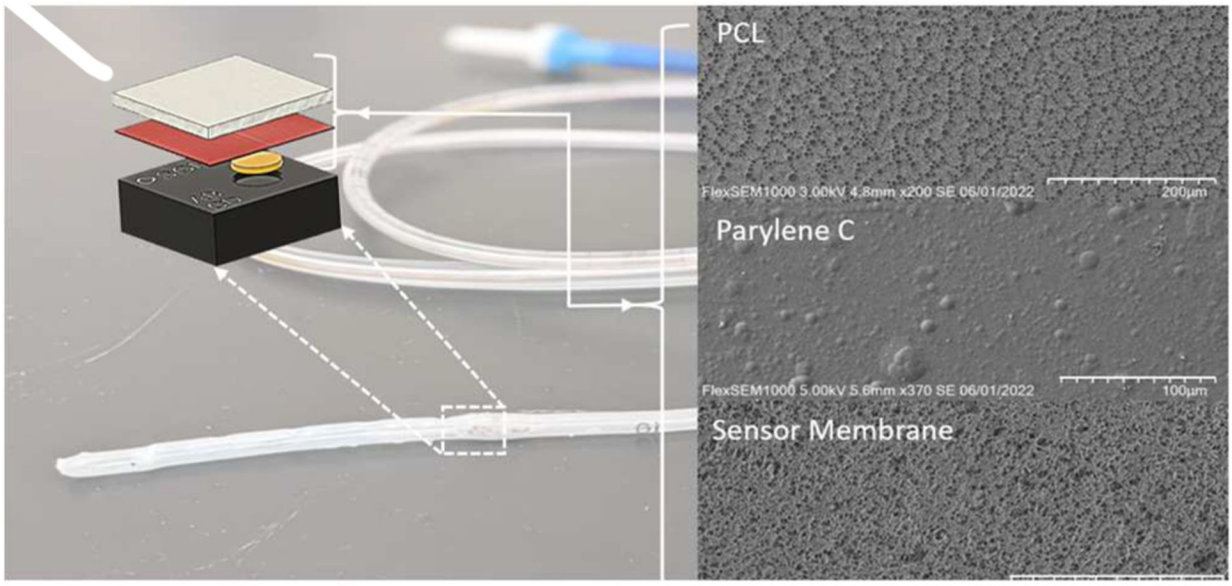

Fig. 1.

Drawing Optical image and schematic exploded view of the encapsulated NG tube-based gas sensor. Top right to bottomright SEM pictures in order of PCL, Parylene C & Sensor internal membrane. The intrinsic sensor membrane is a highly porous thin film. The Parylene C coating forms a dense polymer network. The PCL coating forms a porous thin film.

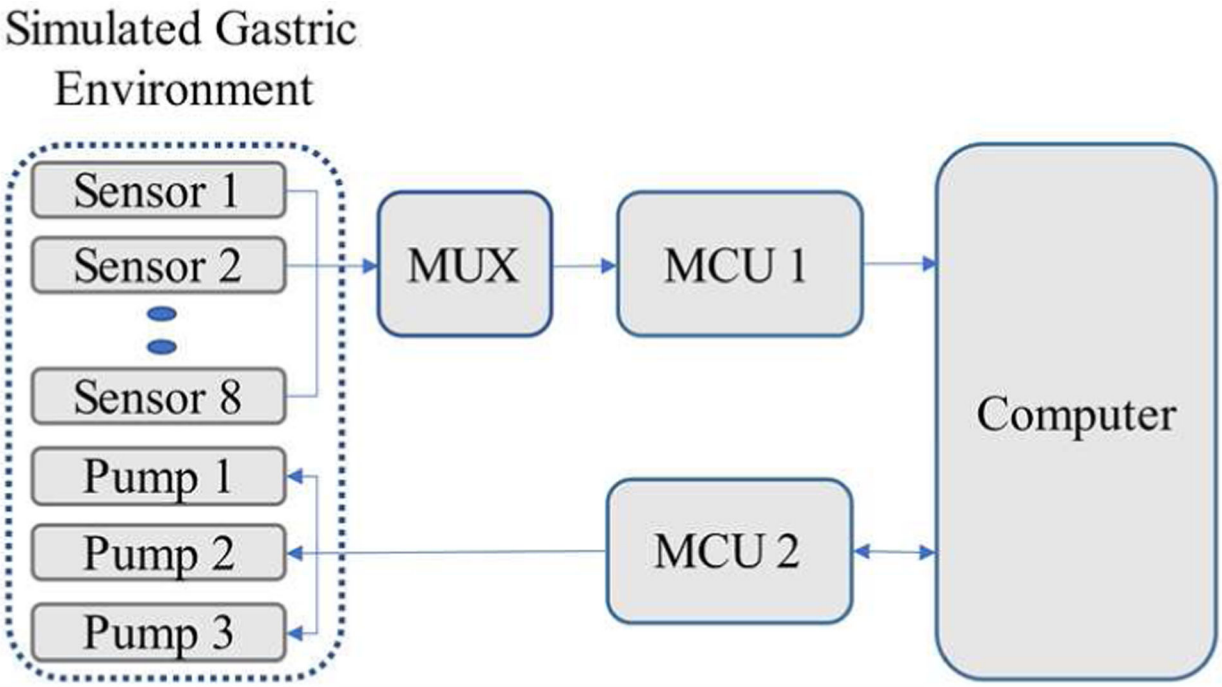

Fig. 2.
Schematic overview of the system.

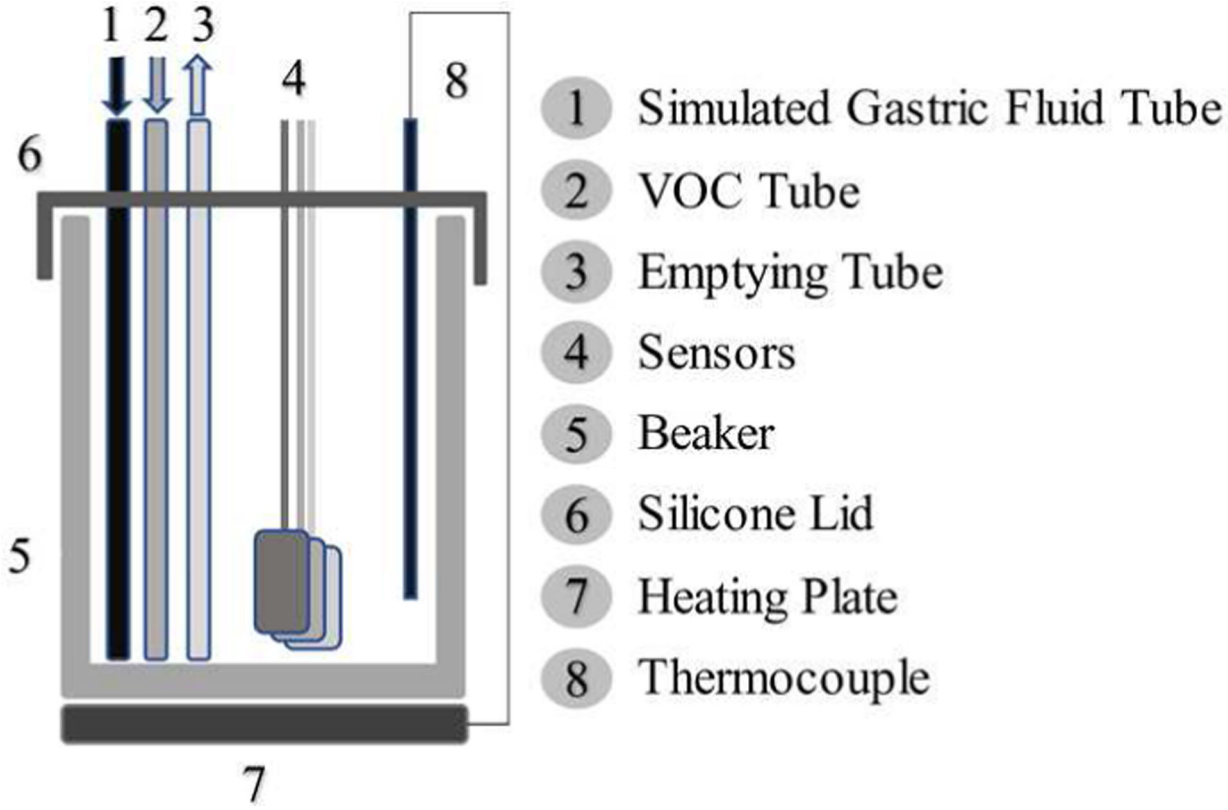

Fig. 3.
Drawing of the simulated gastric environment.

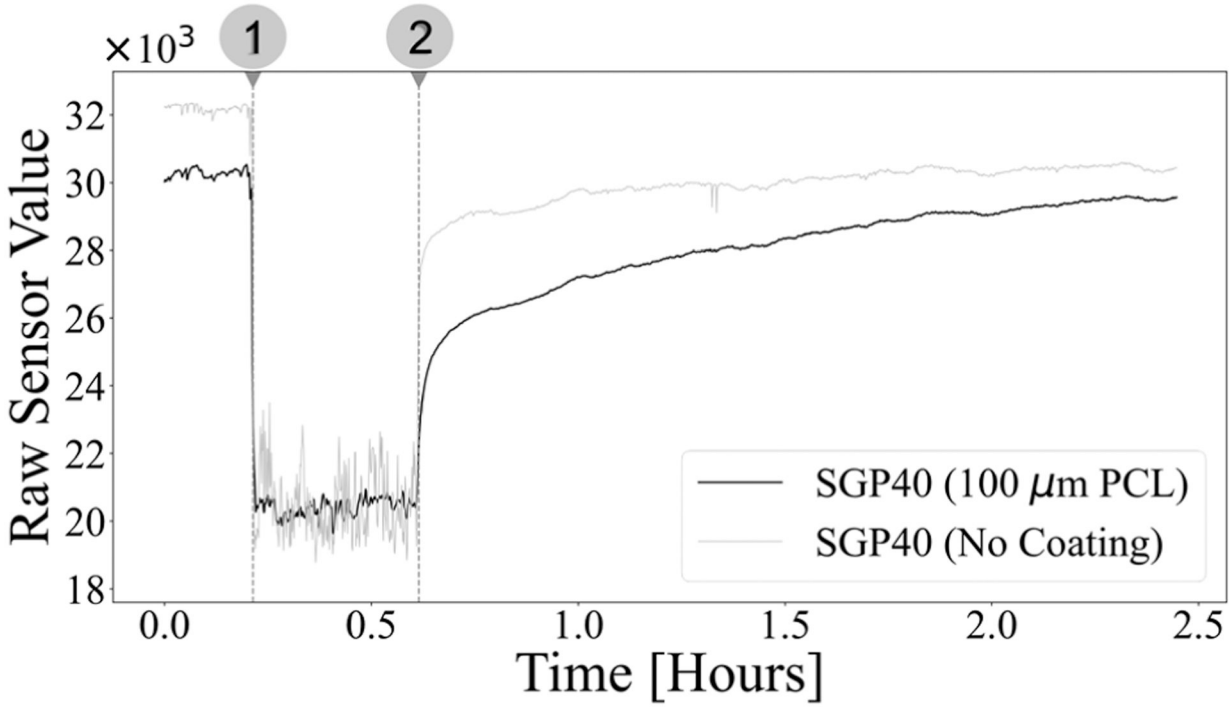

Fig. 4.

Dynamic response of a PCL-coated and uncoated gas sensor when (1) exposed to a VOC solution in air and (2) pulled out from the VOC environment.

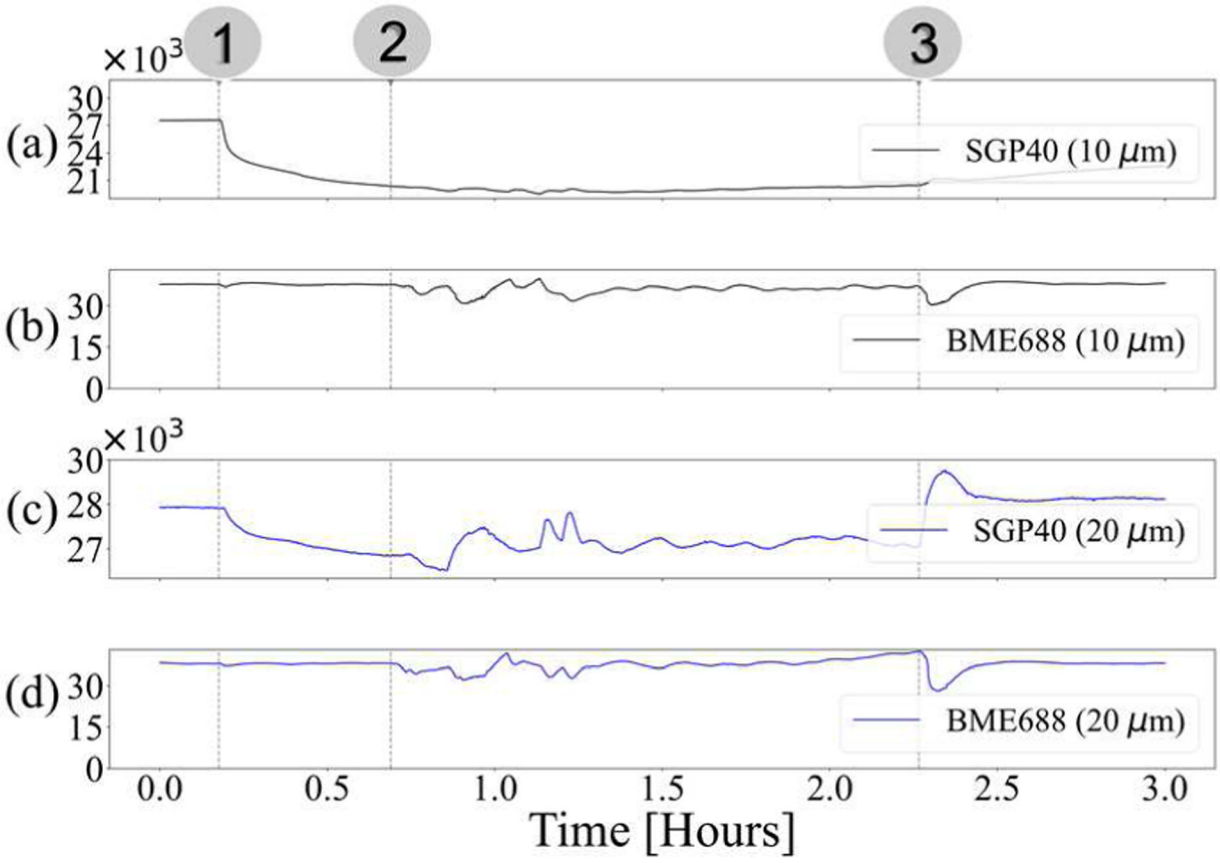

Fig. 5.

The dynamic response of the sensors over 3 hours when (1) a VOC at room temperature is added to the solution, (2) the gastric environment is emptied and (3) the gastric environment is filled with fresh simulated gastric fluid at room temperature. (a) and (c) refer to the SGP40 raw sensor value response, while (b) and (d) are the BME688 temperature responses in degrees Celsius.

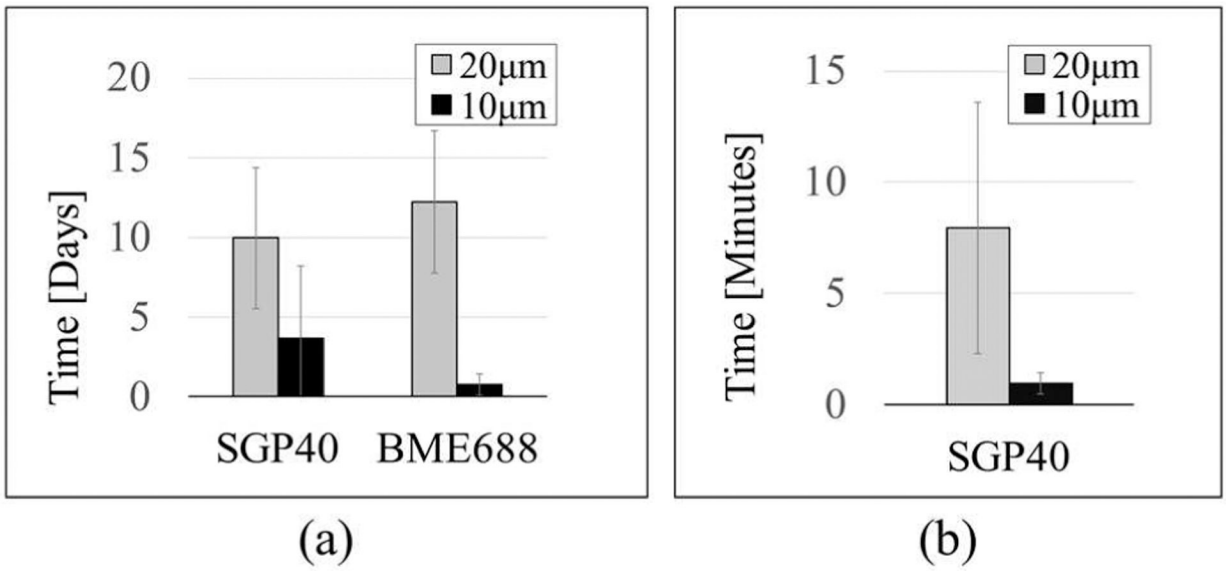

Fig. 6.

(a) lifetime and (b) latency of selected sensors, obtained from at least three sensors for each coating thickness.

TABLE I:

Analysis of the precision of the SGP40 digital raw sensor value after 30 minutes in a VOC solution for different Parylene C coatings. The results were obtained from three sensors for each coating thickness and each sensor was repeated 9 times on average.

Standard Deviation [%]	10 μm	20 μm
Within sensors	1.30	2.10
Between sensors	5.19	3.06