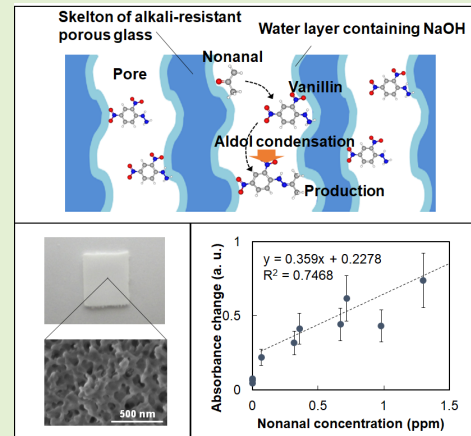


Nonanal Sensor Fabrication Using Aldol Condensation Reaction Inside Alkali-Resistant Porous Glass

Masato Tsujiguchi, Takashi Aitoku, Hironori Takase, and Yasuko Yamada Maruo

Abstract—Monitoring the gases released during breathing or via the skin has gained significance towards diagnosing diseases. In this study, a sensor chip capable of detecting nonanal gas, which is known to be a marker of lung cancer, was developed. The gas detection agent used was vanillin, which underwent aldol condensation with nonanal in the presence of a basic catalyst, resulting in the formation of an unsaturated aldehyde. Porous glass was used as the reaction field to carry the detection agent. Alkali-resistant porous glass was chosen because conventional porous glasses show low durabilities under basic conditions, as they primarily consist of SiO_2 . Nonanal can be detected through changes in the absorption spectrum of the sensor. An accumulate-type sensor was used in this study, which exhibited a linear relationship between the degree of absorption changes at 470 nm and nonanal concentration in the 60 ppb–1.3 ppm range. Therefore, this biological marker gas sensor is effective for the early diagnosis of diseases. The alkali-resistant porous glass sensor chip exhibited a higher degree of absorption change than the conventional porous glass sensor chip.

Index Terms—Aldol condensation, alkali-resistant glass, gas sensor, nonanal, porous glass, vanillin.



I. INTRODUCTION

ADVANCED preventive care is vital for maintaining health and controlling overall medical expenses in societies with aging populations. With the increasing emphasis on healthcare in economically developed societies, breath examination is gaining attention as a novel medical examination approach because it is noninvasive, easy, and quick [1]–[8]. In Table I, examples of biomarkers of the gases present in human breath are listed. Lung cancer has one of the highest mortality rates among cancers because it cannot be discovered early by conventional methods such as thoracic X-ray examination [9]. Several studies have been conducted to detect lung cancer by breath examination, and nonanal, which is a marker for lung

cancer, has been reported to be one of the gases present in the breath [2]–[4]. The concentration of nonanal in human breath is of the order of parts per billion (ppb) [2]. Gas chromatography is often used to measure low concentrations of nonanal; however, this system is large, expensive, and requires special technical knowledge to analyze the results. For rapid and easy medical breath examination, handheld sensors are needed. Several studies have been conducted on nonanal sensors [10]–[16]. Among them, current semiconductor gas sensors are compact and mass-producible, but have poor gas selectivity and sensitivity for high-molecular-weight gases [10]–[12]. A more sensitive semiconductor gas sensor using a nanotube single crystal as a sensitive agent is reported, which also has low gas selectivity [13]. Therefore, pretreatment to separate nonanal from other gases is required. The quartz crystal microbalance (QCM) sensor consumes lower energy. However, it is not effective for light materials such as gas molecules because it measures a mass variation of the electrode before and after adsorbing the gas. It has achieved no more than several decades of ppm order sensitivity for aldehyde [14], [15]. In contrast, a chemosensitive sensor using a gas chromatography material and carbon black is a quick and structurally simple detection method, but also shows poor gas selectivity [16].

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TABLE I
GAS SPECIES IN THE BREATH AND THE PROBABLE DISEASE

Gas species	Main diseases
Nonanal[2-4]	Lung cancer
Decanal[5]	Ovarian cancer
Acetaldehyde[6]	Cancer, Alcohol drinking
Acetone[7]	Diabetes mellitus
2-pentanone[8]	Chronic obstructive pulmonary

This study focused on a porous glass gas sensor. Owing to their high selectivity and sensitivity, porous glass gas sensors were used to develop medical breath analyzers, which was the objective of this study.

Porous glass is a glass material with open nano-pores and is used in various applications such as gas separation filters [17], catalysts [18], enzymes [19], and chromatography filler material [20]. In recent times, because of its large specific surface area, porous glass has exhibited great potential as a reaction field in sensors. In particular, porous glass is effective for the development of optical sensing platforms because it mainly consists of silica [21], which does not absorb light in a broad wavelength range or self-fluoresce. Owing to these advantages, porous glass was selected for use as the reaction field between the gas detection agents and target gas, making this sensor a porous gas sensor [22]–[24].

The following describes the details of the porous glass gas sensor [22]–[24]. When the target gas enters the pores, the gas adheres to the water layer formed on the silanol groups on the inner walls of the pores. The gas then reacts with the detection agents to generate a reaction product, which adsorbs light of a wavelength different from that absorbed by the initial agent. Thus, the change in the absorption spectrum enables target gas detection. The sensor detects a wide range of gaseous species when the appropriate gas detection agent is chosen. In addition, the sensor possesses high sensitivity because it uses transmitted light. Moreover, the absorption spectrum depends on the reaction products and differs according to the gaseous species; therefore, the porous glass gas sensor has high gas selectivity. Owing to the presence of silanol groups on the surfaces of the inner walls of the pores with an extremely high specific surface area and high light transmission ability, porous glass is suitable for the reaction field of this sensor.

To detect lower concentrations of nonanal, we employed the aldol condensation reaction [25]. This is considered to be a sensitive aldehyde gas detection system under simple alkali-catalysis conditions in the development of the porous glass nonanal sensor.

However, conventional porous glass is not resistant to basic conditions [26]; therefore, improving the porous glass resistance to degradation is required to minimize the degradation of the porous glass-supported agent. We addressed these limitations by attempting to study the composition of the porous glass to develop its alkaline resistance.

Further, we developed the nonanal sensor using the aldol condensation reaction, and investigated the effects of using the alkali-resistant porous glass as the aldol condensation reaction

field. Additionally, we reported on the nonanal sensing ability of the sensor.

II. MATERIALS AND METHODS

A. Nonanal Sensing Reaction and Solution System Evaluation

To clarify the spectra of vanillin, nonanal and the reaction product, the solution system was tested as follows. By dissolving vanillin (0.01 g, Wako special grade, FUJIFILM Wako Pure Chemical Corporation, Japan) in deionized water (10 mL), a 1% vanillin aqueous solution was prepared. By dissolving sodium hydroxide (0.4 g, special grade, Kanto Chemical Co., Inc., Japan) in deionized water (20 mL), a 5 mol/L NaOH aqueous solution was prepared. The prepared vanillin and NaOH solutions were mixed. Subsequently, 10 mL of a nonanal ($\text{CH}_3(\text{CH}_2)_7\text{CHO}$, Wako 1st grade, FUJIFILM Wako Pure Chemical Corporation, Japan) ethanol solution with the desired concentration was added to the vanillin-NaOH mixture solution. This solution was transferred to an Erlenmeyer flask, which was subsequently sealed and heated at 373 K for 60 min in a water bath. The heated solution was then extracted with 40 mL of toluene (Wako special grade, FUJIFILM Wako Pure Chemical Corporation, Japan) using a separatory funnel. Collection and evaporation of the toluene layer resulted in a white powder. The white powder was dissolved in acetonitrile (Wako special grade, FUJIFILM Wako Pure Chemical Corporation, Japan), and the solution was spectroscopically analyzed via UV-Vis spectroscopy (UH-4150, Hitachi High-Tech Science Corporation, Japan). The UV-Vis spectroscopy measurement ranged from 200–600 nm. Nonanal and vanillin were dissolved in acetonitrile and water, respectively, and the solutions were analyzed spectroscopically within a range of 200–500 nm.

B. Alkali-Resistant Porous Glass Preparation

Porous materials are functional materials used in various applications. In particular, porous glass has unique characteristics, which include pore diameter controllability, diameter range, pore structure, and translucency. Porous glass is typically manufactured by phase separation methods [27], [28].

A phase separation method was used to prepare the porous glass samples. The following describes the details of the phase separation method (Fig. 1). Soda-borosilicate glass was phase-separated into the silica phase and soda-borate phase by heating it beyond the glass transition point. Subsequently, only the soda-borate phase was leached by an acid solution, which produced the pores. The silica phase remained and formed the skeleton. To improve the alkali resistance, we used ZrO_2 in addition to SiO_2 as the porous glass component.

The ingredients for the preparation of the glass were SiO_2 , B_2O_3 , Na_2O , K_2O , Al_2O_3 , CaO , P_2O_5 , and ZrO_2 . K_2O , Al_2O_3 , CaO , and P_2O_5 are the components that affect the desirable phase separation. The ingredients were placed in a platinum melting pot and melted at 1673 K. The molten glass was cast on a steel plate into the shape of a plate and gradually cooled. The glass samples were processed to a size of 10 mm × 10 mm × 0.5 mm and subjected to phase-separation heat treatment at 948 K. The phase-separated

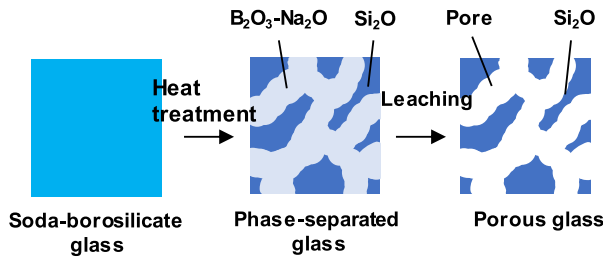


Fig. 1. Manufacturing of porous glass using the phase separation method.

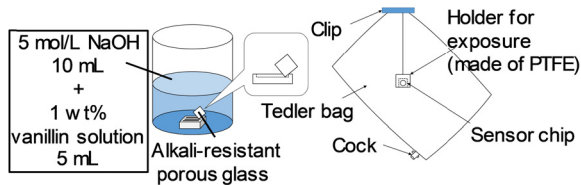
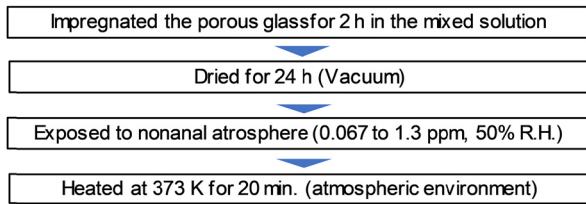


Fig. 2. Illustration of nonanal sensor chip preparation and nonanal sensing evaluation.

glass samples were leached by a 1 mol/L nitric acid aqueous solution; subsequently, they were leached by a 1.5 mol/L sulfuric acid aqueous solution. Finally, the glass samples were washed with deionized water.

C. Nonanal Sensor Chip Preparation and Nonanal Sensing Evaluation

The nonanal sensor chip preparation and nonanal sensing evaluation are shown in Fig. 2. The nonanal sensor was prepared by dissolving vanillin (0.05 g) in deionized water (5 mL) to prepare a 1% vanillin aqueous solution. By dissolving sodium hydroxide (2 g) in deionized water (10 mL), a 5 mol/L NaOH aqueous solution was prepared. The two solutions were mixed, and the porous glass sample was immersed in the solution at 298 K for 2 h. The sample was removed and dried at 298 K for 24 h under a vacuum to obtain the sensor chips. The absorption spectra and morphology of the sensor chips were analyzed by UV-Vis spectroscopy and field emission scanning electron microscopy (SU-8220, Hitachi, Ltd. Japan), respectively.

The UV-Vis spectroscopy measurement ranged from 350–650 nm. The scanning electron microscopy (SEM) observation was conducted without sample deposition, and the acceleration voltage was 1.6 kV. In addition, a nitrogen adsorbent with a surface and pore size analyzer (Quadrastorb SI, Anton-Paar, Austria) was used to measure the pore size distributions of the sensor chip and porous glass before supporting the gas detection agents. Nonanal sensing evaluation was conducted as follows. A 50 L Tedler bag (1-2711-08,

TABLE II
MANUFACTURING OF POROUS GLASS USING THE PHASE SEPARATION METHOD

	Fig. 7		
	(a)	(b)	(c)
Exposure atmosphere			
Nonanal (ppm)	2.6	1.3	0.067-1.3
Water		50% RH	
Exposure time	4 h	4,-24 h	24 h
Exposure temperature		298 K	
Heating condition			
Temperature		373 K	
Time		1 h	
Compared wave length	-	470 nm	470 nm

As one, Japan) was filled with nitrogen (50 L, industrial grade, Iwatani Corporation, Japan). Various quantities of nonanal (25, 120, 140, 250, 280, 380, and 500 μ L) were diluted to 20 mL with ethanol. The resultant nonanal solutions (40 μ L each) were placed in the Tedler bag to obtain 0.067, 0.32, 0.36, 0.67, 0.72, 0.98, and 1.3 ppm nonanal atmospheres. The relationship between exposure time and sensitivity was evaluated at 1.3 ppm. The calibration curve was evaluated from 0.067 ppm to 1.3 ppm. Deionized water (575 mL) was placed in the Tedler bag to increase the relative humidity to 50%. The sensor chip was wrapped in a bag composed of a Teflon filter membrane (T020A, Advantec Toyo, Japan) with a 0.2 μ m pore size, which was then suspended in the Tedler bag with a Teflon thread for the prescribed time. Subsequently, placing the sensor chip in a polypropylene container and heating it in a convection oven at 373 K for 1 h promoted the aldol condensation reaction. After nonanal exposure and heating, the sensor chip absorption spectrum was obtained by UV-Vis spectroscopy. To evaluate the relationship between exposure time and sensitivity, the nonanal sensor chip was exposed to a nonanal gas for 4, 15, and 24 h. The exposure time used for calibration curve evaluation was 24 h.

The metrological parameters are summarized in Table II.

D. Evaluation of the Effect of Porous Glass Alkali Resistance

The alkali resistance measurement of the prepared glass was performed as follows: (i) the initial weights of the glass samples were measured after heating the samples at 453 K for 3 h under a vacuum, (ii) the samples were then immersed in 0.5 mol/L aqueous sodium hydroxide at 348 K for 40 min, and (iii) after drying the samples, their weights were measured under the aforementioned conditions. The weight losses per unit specific surface area of the samples that were immersed in the alkaline aqueous solution were obtained.

To probe the origins of the alkali sensitivity and resistance of the conventional and the treated porous glass, the amounts of the reaction product obtained on both samples of the porous glass were analyzed and compared. The amount of reaction

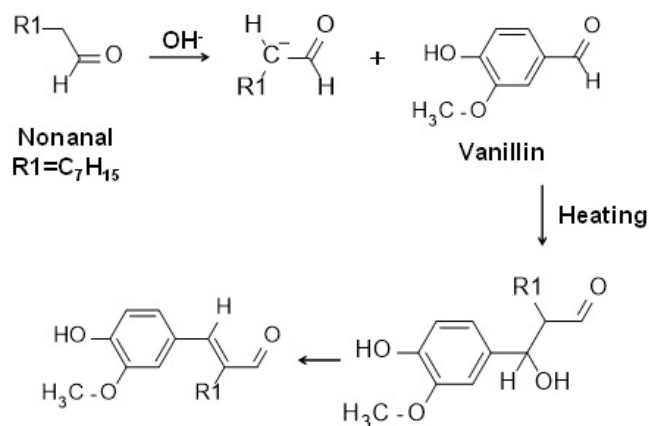


Fig. 3. Aldol condensation of vanillin with nonanal.

product formed upon immersion in the NaOH aqueous solution was evaluated as follows. The sensor chip was immersed in the 0.1 mol/L HNO_3 aqueous solution and stirred using a magnetic stirrer at 298 K for 18 h. The reaction product trapped inside the pores of the porous glass sensor chip was extracted. The obtained extract was then filtered through the Teflon membrane filter (25HP020AN, Advantec Toyo, Japan). Using ICP-AES (730 ES, Agilent Technologies, Inc., US) the amount of Si in the solution was analyzed.

The SiO_2 in the glass did not dissolve in the aqueous HNO_3 solution, and the SiO_2 that reacted with the NaOH dissolved in the aqueous HNO_3 solution.

III. RESULTS AND DISCUSSION

A. Reaction Between Vanillin and Nonanal in the Solution System

Fig. 3 depicts the aldol condensation between vanillin and nonanal under alkaline conditions. Fig. 4(a) depicts the UV-Vis absorption spectra of the mixture of vanillin, aqueous NaOH, and nonanal before and after heating and that of vanillin and nonanal after dilution in acetonitrile and water. Fig. 4(b) depicts the UV-Vis absorption spectra of the water layer obtained after extraction of the toluene layer and the acetonitrile solution containing the white powder obtained from the toluene layer. The background, which increased upon heating, decreased after extraction (Fig. 4(a)). This implied that the product of the aldol condensation between vanillin and nonanal was water-insoluble and was extracted into the toluene. The obtained material of the toluene layer exhibited absorbance in the 400–450 nm range, while vanillin and nonanal did not. This indicated that the new absorption peak represented the product of the aldol condensation between vanillin and nonanal.

B. Nonanal Gas Sensing

1) *Structure of the Sensor Chip*: Fig. 5 depicts the scanning electron microscopy (SEM) images of the porous glass before supporting the gas detection agents and the porous glass nonanal gas sensor chip. Before supporting the gas detection agents, precipitation of the SiO_2 colloid was observed inside the pores. As shown in Fig. 5(b) and (c), after supporting the

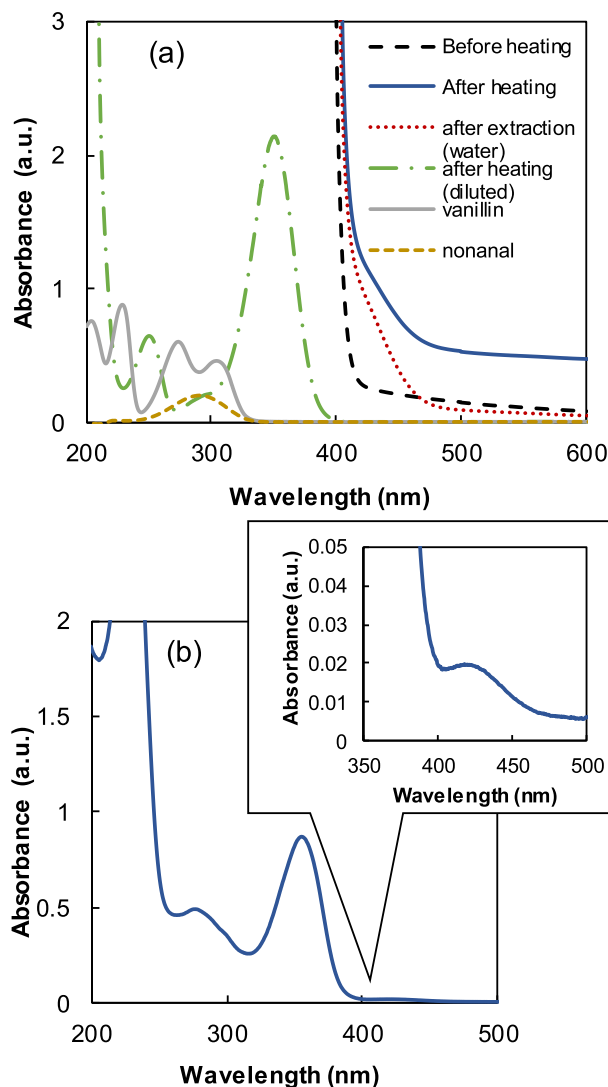


Fig. 4. (a) Absorption spectra of the vanillin and aqueous NaOH mixed solution, nonanal before and after heating, and water layer after extraction of the toluene layer. The heating temperature was 373 K, and the heating time was 60 min. (b) Spectrum of the acetonitrile solution containing the white powder obtained from the toluene layer.

gas detection agents, the glass exhibited a skeletal structure caused by the spinodal phase separation. Further, precipitation of the SiO_2 colloid was not observed because the SiO_2 colloid was eluted by the NaOH in the agent. Moreover, the skeleton of the developed porous glass, which has alkali resistance, was not eluted by NaOH. The SEM results revealed an approximate pore size of 50–70 nm, and the structure covered the gas sensor sample homogeneously (Fig. 5(c)).

Fig. 6 depicts the pore size distributions of the porous glass before supporting the gas detection agents and the porous glass nonanal gas sensor chip. The pore size distributions were obtained from the desorption isotherm using the Barrett, Joyner, and Halenda method [29]. The pore size distribution of the porous glass before supporting the agents showed that two kinds of pores existed in the original porous glass: fine and coarse pores. The fine pores exhibited a peak size at 4 nm, and the coarse pores displayed a peak at 65 nm. The fine pores were formed due to the SiO_2 colloid precipitation, while

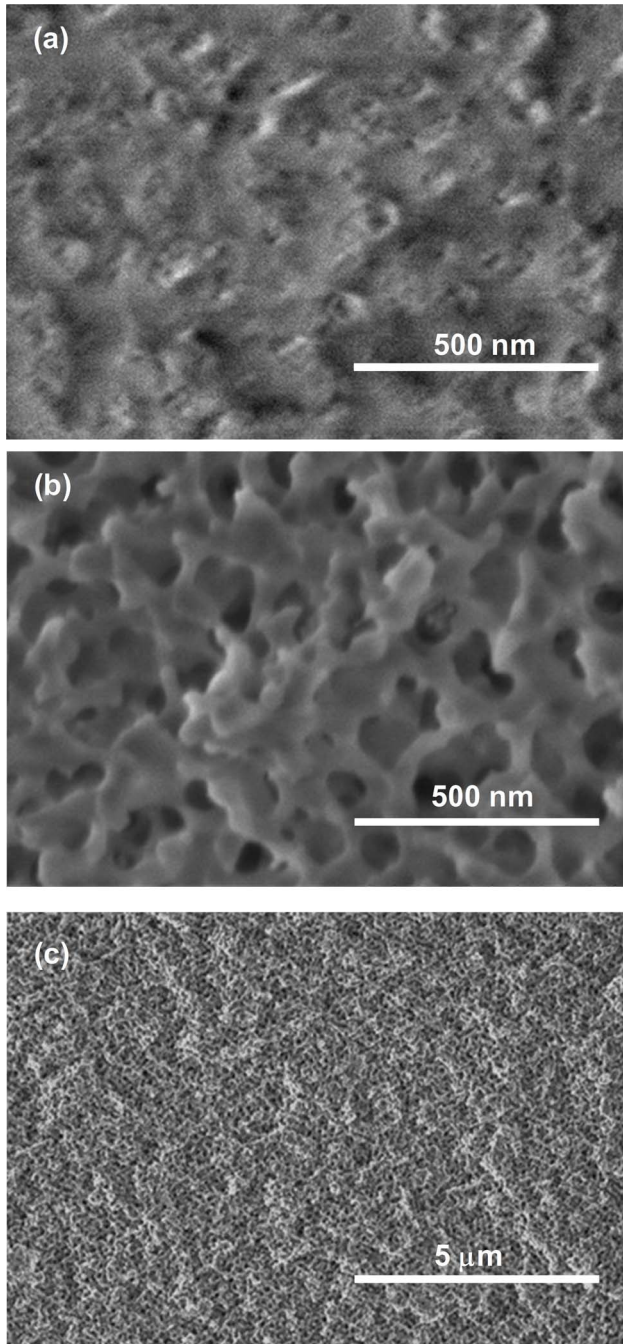


Fig. 5. SEM photographs of the microstructure of (a) the alkali-resistant porous glass before supporting the gas detection agents, (b) the nonanal sensor chip after supporting the agents, and (c) the wide range image of (b).

the coarse pores were formed due to phase separation. After supporting the gas detection agents, only the coarse pores were observed because the SiO_2 colloid was eluted by the NaOH in the agent, as mentioned previously.

The pore size distributions were in agreement with the SEM images. The porous glass nonanal gas sensor chip had a narrow pore size distribution, and the median pore diameter was approximately 65 nm, which was sufficiently large considering the mean free path of the nonanal gas. The mean free path of gas i in the mixture gas is written as follows [30], considering

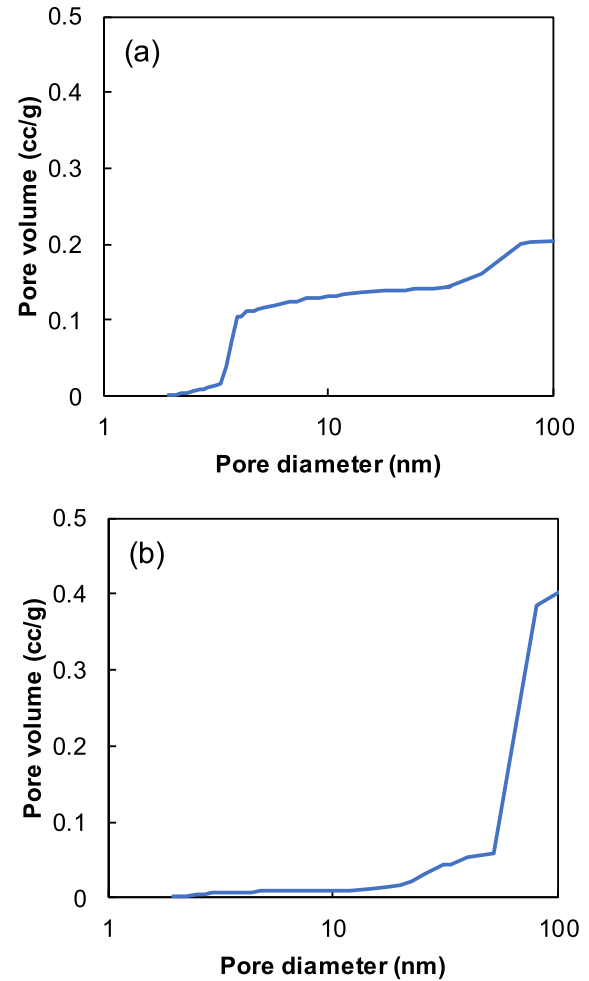


Fig. 6. Pore size distributions of (a) alkali-resistant porous glass before supporting gas detection agents and (b) nonanal sensor chip after supporting the agents.

the Maxwell-Boltzmann approximation:

$$L_i = \left[\sum_{j=1}^q S_{i,j} n_j \left(1 + \frac{m_i}{m_j} \right)^{1/2} \right]^{-1},$$

where S_{ij} is the mutual collision cross-section of gases i and j , n_j is the number density of gas j , and m_i and m_j are the masses of gases i and j , respectively. $S_{ij} = \pi r_{ij}^2 = \pi [1/2(r_i + r_j)]^2$, where r_i and r_j are the radii of gases i and j , respectively. n_j is given by the state equation, $n = P/kT$. The calculated value of the mean free path of nonanal, based on this formula, was approximately 9 nm. This result showed that the porous glass sample contained several sufficiently large pores for nonanal gas to diffuse inside the pores.

The porosity was approximately 47%, obtained from the pore volume of 0.4 mL/g, supposing that the porous glass framework density was 2.2 g/cm³. The specific surface area obtained using the Brunauer-Emmett-Teller method [31] was approximately 12 m²/g. The Brunauer-Emmett-Teller method is as follows: The molecule, which has a known adsorption occupied area, is adsorbed on the pore surface at 77 K. The surface area is then obtained from the adsorption amount.

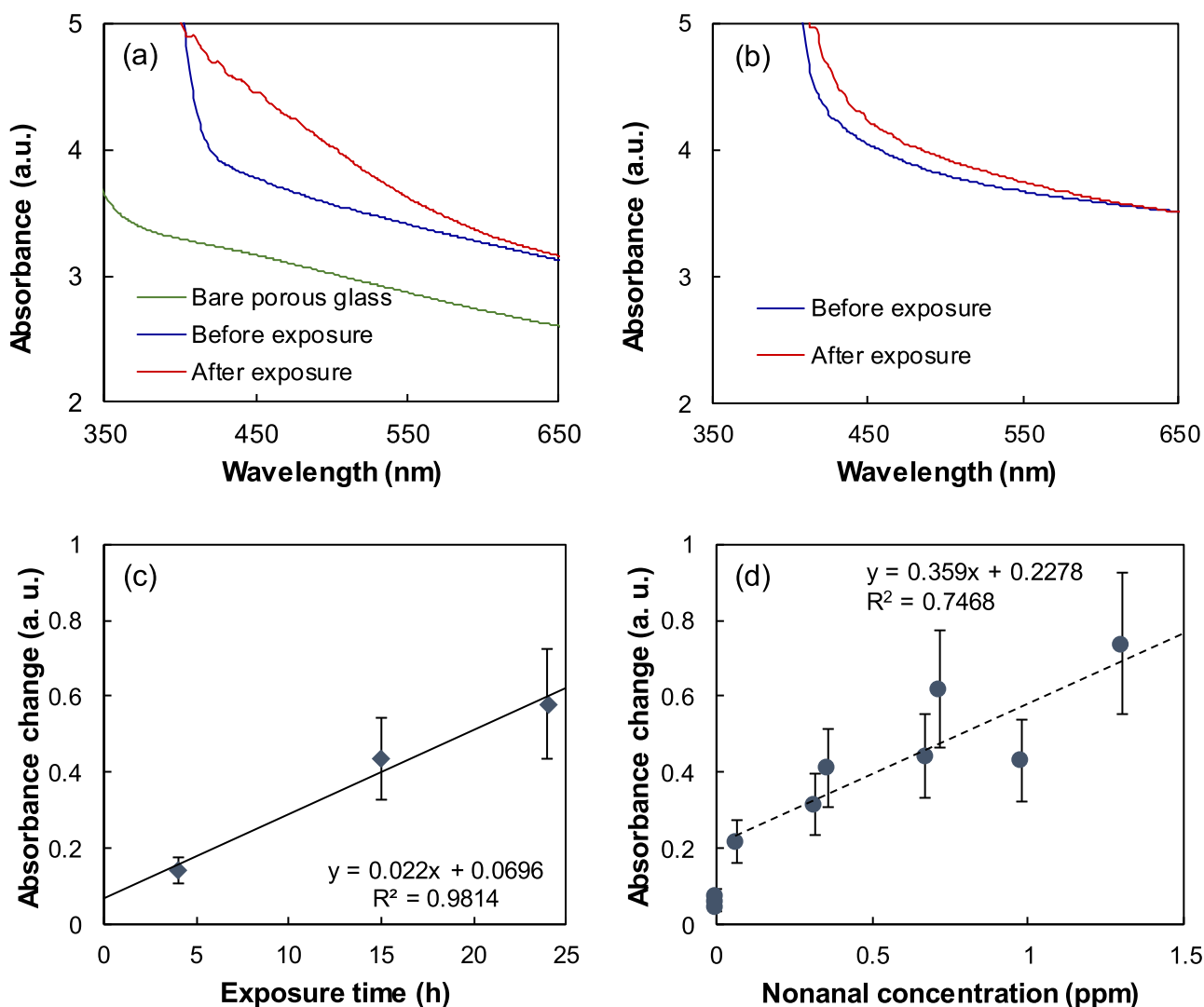


Fig. 7. Absorbance spectra of nonanal sensor chips composed of (a) alkali-resistant porous glass and (b) conventional porous glass before and after nonanal exposure. The nonanal concentration was 2.8 ppm, and the exposure time was 4 h. (c) Relationship between exposure time and absorption change at 470 nm. The experiment was conducted at a nonanal concentration of 1.3 ppm. (d) Relationship between nonanal concentration and absorbance change at 450 nm. The exposure time was 24 h.

2) Reaction Between Vanillin and Nonanal Gas on the Sensor Chip: Fig. 7(a) depicts the absorption spectra of the bare porous glass and the porous glass sensor chip composed of the alkali-resistant porous glass, and the conventional porous glass before and after nonanal exposure and heating. The nonanal concentration, exposure time, and heating condition after nonanal exposure were 2.6 ppm, 4 h, and 373 K for 1 h, respectively. The upper limit of the measured absorbance spectrum was 5 a.u. The bare porous glass had no absorbance peak except for the Rayleigh scattering below 360 nm, which was due to the microstructure (Fig. 7(a)).

The absorption in the wide wavelength range (350–650 nm) is relatively high due to Mie scattering of the microporous structure of the bare porous glass. After supporting the gas detection agents, no absorption peak was observed below 400 nm, which could be attributed to the vanillin supported inside the pores. Absorption in the wide wavelength range

(400–650 nm) attributed to the Mie scattering increased, relative to the bare porous glass. This was because the NaOH permeated inside the pores and formed fine precipitates with the increase in Mie scattering. The spectrum change after supporting the gas detection agents showed that the gas detection agent layer was formed inside the porous structure.

After nonanal exposure and heating, the absorption in the 400–550 nm wavelength range increased, implying the occurrence of aldol condensation between vanillin and nonanal. The absorbance change was approximately 1.0 a.u., and the absorption was in the same range as that of the reaction product in the solution system. Although the product of the aldol condensation was water-insoluble and aggregated in the solution, it dispersed into the pores of the porous glass and the absorbance change could be measured by the porous glass sensor.

Fig. 7(b) depicts the absorption spectra of the conventional porous glass sensor chip before and after nonanal exposure and heating. The variation in the absorption amount by the sensor chip composed of alkali-resistant porous glass was larger than that of the chip composed of conventional porous glass, indicating that the use of the alkali-resistant porous glass for the fabrication of the nonanal sensor based on the aldol condensation reaction resulted in higher sensitivity. The reason is described in Section III.C.

Fig. 7(c) depicts the relationship between the exposure time and absorption change at 470 nm. The absorption increased with increasing exposure time, indicating a linear relationship between the storage of the nonanal (the product of the gas concentration and exposure time), and absorption change. The amount of nonanal adsorbed on the inner walls of the pores increased with time, increasing the nonanal concentration in the atmosphere. The concentrations of the gas detection agents (vanillin and NaOH) in the pores were sufficient to achieve linearity in the formation and detection of the aldol condensation product over time, and with nonanal concentration.

As mentioned previously, the developed sensor could be considered as an accumulate-type sensor. It continues to accumulate nonanal and shows the designated time-integrated value. This suggested that it can be used not only for measuring the gaseous components in breath, but also for accumulating gases from the human body such as the skin.

3) Calibration Curve: Fig. 7(d) depicts the relationship between the nonanal concentration in the atmosphere and the absorption change at 470 nm. The absorption change increased with increasing nonanal concentration, and a linear relationship was observed between the nonanal concentration and absorption change. As mentioned previously, the porous glass sensor chip was an accumulate-type sensor. As the porous glass had a large specific surface area, it exhibited a high gas adsorption ability and gas sensitivity. Furthermore, the amount of nonanal gas accumulated in the sensor chip (the product of the gas concentration and exposure time) was proportional to the nonanal concentration because the sensor chips were exposed to nonanal gas for fixed times. This indicated that the developed gas sensor could be used for quantitative evaluation.

Regarding the blank measurement, water and ethanol, it suggested that for dilute concentrations below 50 ppb, the change in nonanal concentration and absorbance showed a logarithmic relation similar to the porous glass formaldehyde sensor [11].

The sensitivity of the developed sensor was analyzed. The calibration curve showed a one-to-one correspondence in the nonanal concentration range of 67 ppb to 1.3 ppm (Fig. 9), indicating that the sensor can be used to measure nonanal concentrations of the order of several decades of parts per billion. This result was equivalent to that obtained for semiconductor gas sensors, wherein the detection range was greater than 50 ppb [4]–[6].

The standard deviation and variation coefficient obtained from the multiple blank measurements were 0.015 and 25%, respectively. The three-sigma value was 0.045, which corresponded to the limit of detection (LOD) of the absorption

change as a result of considering the variation in multiple measurements. In this developed sensor chip, the absorption change per unit concentration (ppm) was approximately 0.37 a.u.; therefore, the absorbance change of 0.045 corresponded to 125 ppb of nonanal. As a result, the LOD of the nonanal concentration was considered to be 125 ppb.

Furthermore, the photometric accuracy of a spectrometer is generally not higher than 0.005 a.u., when the absorbance is less than 1 a.u. [32]. This indicated that if the developed sensor variation, which might be related to the variation of the porous structure or detection agents decreased, the sensor could reach a lower LOD of approximately 14 ppb. Therefore, the developed sensor was suitable for gas detection across a wide nonanal concentration range, potentially from 14 ppb to 1.3 ppm.

The absorbance of the developed sensor chip was approximately 3.8 a.u. because the pore diameter was larger than the optimum value for nonanal sensing. Additionally, certain absorption values were also derived from the gas detection agents. This issue could be addressed by reducing the absorbance of the sensor chip, which could be achieved by reducing the pore size, improving the dispersibility of the gas detection agent, or reducing the alkali concentration. Among these approaches, reducing the pore size might be most effective for nonanal sensing because the pore size obtained in this study was relatively large for effective adsorption of the nonanal gas molecule.

The selectivity of the sensors was investigated using acetone, which is a marker gas for diabetes mellitus in breath [7]. The sensitivity of acetone was 0.004 per ppm, which was smaller than that of nonanal by two orders of magnitude. It was considered that as acetone does not contain an aldehyde group, the aldol condensation reaction did not occur.

The selectivity of the sensors towards formaldehyde was also investigated, which is one of the aldehyde gases present in human breath [33]. The sensitivity of formaldehyde was 0.17 per ppm, and that of nonanal was 0.36. It was apparent that the sensor was not able to efficiently separate nonanal and formaldehyde in this study. The sensor developed by us previously, to detect formaldehyde, might be effective to separate formaldehyde from nonanal [23].

Saliva examination can play a major role in non-invasive cancer examination. Intraoral cancers have been detected by evaluating the microRNAs in the saliva [34], and colon cancer can potentially be detected by investigating the extracellular vesicles [35]. However, saliva contains significantly fewer biomarkers relative to blood and often contains food residues, resulting in inaccurate test results.

Furthermore, similar to the breath-gas method, measuring gases from urine could also be a non-invasive and simple method for cancer detection [36], [37]. However, the method fails to detect the type of cancer.

The advantage of using the breath gas sensor developed in this study is that it only utilizes common ingredients, such as vanillin and NaOH. In addition, it does not require a large-scale manufacturing apparatus, thereby potentially reducing the production cost.

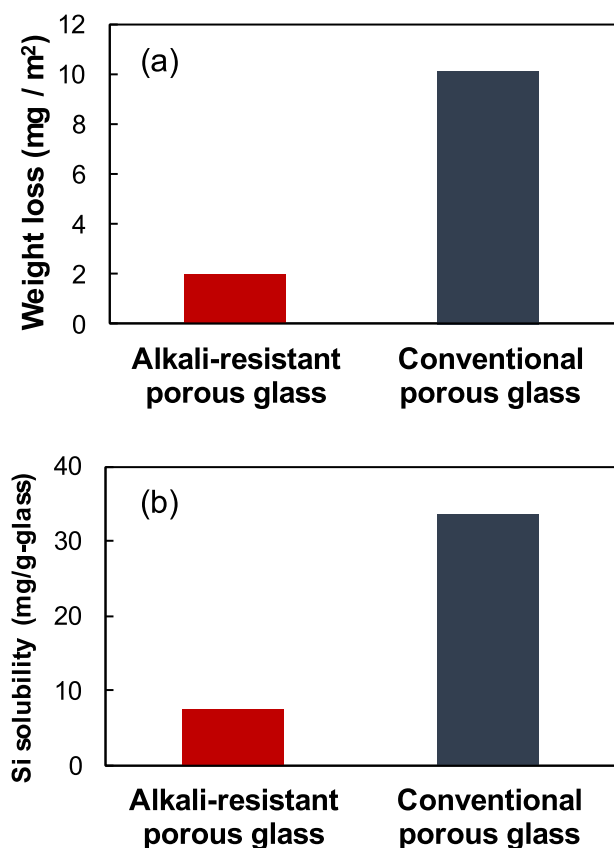


Fig. 8. (a) Relationships between elution time and weight loss of alkali-resistant porous glass and conventional porous glass. (b) Si solubilities of porous glass sensor chips composed of alkali-resistant porous glass and conventional porous glass.

C. Effect of Alkali Resistance of Porous Glass

Fig. 8(a) shows the results of the alkali resistance test. Conventional porous glass without ZrO₂ was also tested. The weight loss of the alkali-resistant porous glass was significantly lower, approximately 20% of that of the conventional porous glass. This improved alkali resistance was attributed to the known beneficial effects of ZrO₂ in imparting alkali resistance to glass [38]–[40]. For example, glass fibers containing ZrO₂ have well-known applications as alkali-resistant glass fibers in reinforcing Portland cement [41]. The results confirmed that even in the porous glass system, the alkali resistance observed in the glass fiber could be realized by adding ZrO₂ to the glass components.

Fig. 8(b) depicts the amount of Si extracted from the nonanal sensor chips composed of the alkali-resistant porous glass and conventional porous glass. A 0.1 mol/L aqueous HNO₃ solution was used to extract the Si from the sensor chip. It was almost impossible to dissolve Si in the glass network with the diluted aqueous HNO₃ solution. Therefore, the Si extracted in this case, originated from the porous glass and NaOH reaction product. The Si extracted from the alkali-resistant porous glass was 20% of that obtained from the conventional porous glass. This value corresponded reasonably well with the aforementioned results of the alkali resistance test, which showed that the weight loss of the alkali-resistant porous glass was 20% of that of the conventional porous glass.

It was likely that sodium silicate hydrate was the reaction product because SiO₂ was the dominant component of the porous glass. Sodium silicate hydrate is well-known to polymerize with increasing density [40]. In the developed system, the gas detection agent with a concentrated alkaline aqueous solution was supported on the porous glass at 298 K without stirring. Furthermore, the solution quantity was not sufficient; hence, diffusion of the sodium silicate hydrate product was expected to be extremely slow. Thus, it could be deduced that sodium silicate hydrate concentrated inside the pores, and it was known that under such conditions sodium silicate hydrate tended to polymerize. Upon polymerization, the sodium silicate transformed into a gel-like product and blocked the pores across several dozen nanometers of the porous glass. With the pores blocked, the diffusion of the detection agents into the porous glass was prevented. Therefore, the facile production of the gel-like sodium silicate polymer on the conventional porous glass resulted in its lower sensitivity, as compared to the alkali-resistant glass. Consequently, the developed alkali-resistant porous glass expanded the choices of detection agents.

CONCLUSION

A nonanal sensor chip was produced using alkali-resistant porous glass. For gas detection, the aldol condensation reaction between vanillin and nonanal was employed. The results of the solution system test showed that the product of the reaction between vanillin and nonanal had an absorption peak in the 400–450 nm range, wherein vanillin and nonanal did not absorb.

The sensor chip was confirmed to be an accumulate-type sensor. The concentration of the nonanal gas and absorption change of the sensor chip had a linear relationship, indicating that the sensor chip could be used for the quantitative evaluation of nonanal concentrations.

The developed alkali-resistant porous glass had high alkali resistance and showed a lower weight loss (20 % of that of the conventional porous glass). The superior alkali resistance was attributed to the use of ZrO₂, which was effective in imparting alkali resistance to the glass, as is conventionally observed in other glass fibers. The sensitivity of the sensor chip produced using the alkali-resistant porous glass was higher than that of the sensor fabricated using the conventional porous glass. It was assumed that the gas detection agent was homogeneously supported inside the pores. A small amount of the reaction product, formed by the reaction between the glass and NaOH likely interfered with the diffusion of the agent inside the pores by forming a gel-like product, which could also occur in the conventional porous glass.

Biomarker gases include different materials and reflect the corresponding bio-information. To utilize the valuable information of biomarker gases, the gas sensor requires high portability, sensitivity, and selectivity. This work has the potential to deliver these requirements. Specifically, the aldol condensation, under a basic pH environment, in alkali-resistant porous glass was achieved, unlike in conventional porous glass. This resulted in higher sensitivity to aldehyde gas, which is a major biomarker gas candidate for lung cancer detection.

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