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Abstract. Smart toilets could be used to monitor different components of urine in daily life for early detection of lifestyle-related diseases and prompt provision of treatment. For analysis of biological samples such as urine by mid-infrared spectroscopy, thin-film samples like liquid cells are needed because of the strong absorption of midinfrared light by water. Conventional liquid cells or fixed cells are prepared based on the liquid membrane method and solution technique, but these are not quantitative and are difficult to set up and clean. We generated an ultrasonic standing wave reflection plane in a sample and produced an ultrasonic liquid cell. In this cell, the thickness of the optical path length was adjustable, as in the conventional method. The reflection plane could be generated at an arbitrary depth and internal reflected light could be detected by changing the frequency of the ultrasonic wave. We could generate refractive index boundaries using the density difference created by the ultrasonic standing wave. Creation of the reflection plane in the sample was confirmed by optical coherence tomography. Using the proposed method and midinfrared spectroscopy, we discriminated between normal urine samples spiked with glucose at different concentrations and obtained a high correlation coefficient. © The Authors. Published by SPIE under a Creative Commons Attribution 3.0 Unported License. Distribution or reproduction of this work in whole or in part requires full attribution of the original publication, including its DOI. [DOI: [10.1117/1.JBO.23.5.050503](https://doi.org/10.1117/1.JBO.23.5.050503)]

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1 Introduction

Early treatment is important in the prevention of lifestyle-related diseases, such as diabetes and gout.¹ Smart toilets that could measure glucose and protein in urine in daily life are of interest in this area. To date, smart toilets can only control cleaning and measure the volume of urine using flow rate sensors, motion detectors, and other technology.² Currently, there is no sensor that can be installed in a toilet and measure different components of interest in urine. If glucose or protein is present in urine, it is possible that the person has diabetes or chronic kidney disease.^{3,4} Early detection of these diseases by smart toilets in daily life could prompt an individual to seek treatment at an early stage of the disease.^{5,6} Many approaches have been investigated for smart toilets and noninvasive blood glucose sensors, with most using near-infrared spectroscopy^{7,8} and wavelengths from 800 to 1500 nm. Near-infrared light can pass through a sample more easily than midinfrared light because it is absorbed less by water.⁹ Therefore, near-infrared spectroscopy can be used for noninvasive analysis of biological samples. However, the near-infrared absorption of glucose is weak because the absorption peak in the near-infrared region appears as an overtone and combination band.¹⁰ Furthermore, it is difficult to identify the absorption peak of glucose because there are also absorption peaks for water, proteins, and hemoglobin in the near-infrared region.^{11,12}

Smart toilets using midinfrared spectroscopy could be used to detect the fundamental vibration of glucose. We have already proposed a small (bean-sized) midinfrared Fourier spectroscopic imager.¹³ However, because midinfrared light is absorbed strongly by water, this imager requires thin-film samples with thicknesses of <100 μm for midinfrared spectroscopy detection of transmitted or reflected light. Conventional liquid cells and fixed cells prepared based on the liquid membrane method and solution techniques are used for optical transmission measurements.¹⁴ Unfortunately, these cells are not quantitative and are difficult to set up and clean.¹⁵ Another option is the attenuated total reflectance method,^{16–18} which uses an evanescent wave that can travel several micrometers into a sample. However, the light must be reflected many times in the attenuated total reflectance prism to meet the required optical path length, and light intensity is an issue because increased reflection leads to increased absorption by the prism and samples.

In this paper, we describe development of an ultrasonic liquid cell, with a reflection plane generated inside the sample by an ultrasonic standing wave, for midinfrared spectroscopy and application to smart toilets [Fig. 1(a)]. We used optical coherence tomography (OCT) to investigate the reflection plane of the ultrasonic standing wave in the sample and applied our method to normal urine samples spiked with different concentrations of glucose. The urine used in the study was collected from a 24-year-old adult male. Additionally, we determined the correlation coefficient for measurement of the glucose concentration to evaluate the feasibility of this method for quantitative measurement of glucose concentrations and the realization of smart toilets. Glucose is typically excreted from blood into urine when the blood glucose level reaches around 180 mg/dL.¹⁹ However, because this level can vary, we instead used the level (50 mg/dL) for a positive result with a urine test strip. For the realization of smart toilets, we believe that a glucose target concentration of 50 mg/dL and measurement accuracy of 30 mg/dL will be relevant.

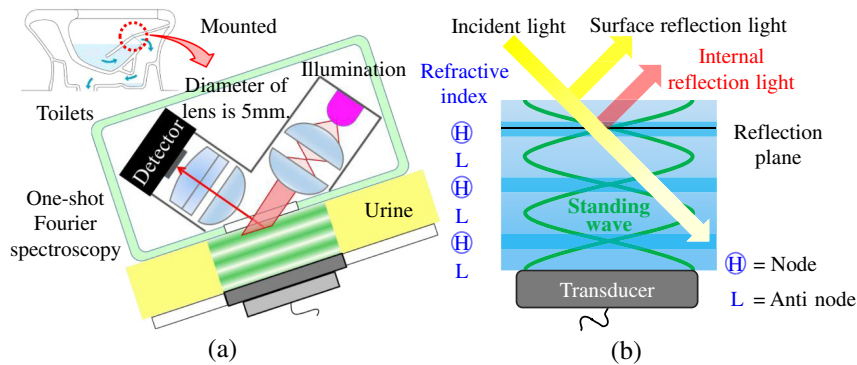


Fig. 1 (a) Schematic diagram of a smart toilet and (b) the liquid cell with variable optical path length.

2 Principles of the Ultrasonic Liquid Cell and Verification Experiments

If a sample is homogeneous, some incident light will be detected as surface reflected light. However, light absorbed within the sample cannot be detected. Therefore, in this method, an ultrasonic standing wave was used to generate refractive index boundaries inside the sample, and internal reflected light was detected at an arbitrary depth [Fig. 1(b)]. Because the ultrasonic wave is a compressional wave, it propagates while generating a density difference within the sample. The refractive index distribution is also stabilized by the ultrasonic standing wave. The incident light is reflected at the node of the ultrasonic standing wave where the refractive index differences are maximized, and it is detected as internal reflected light. The position of the node of the ultrasonic standing wave depends on the frequency of the ultrasonic wave. By manipulating the frequency of the ultrasonic standing wave, we could obtain an arbitrary optical path length in the depth direction.

In this study, the ultrasonic standing wave was generated inside a container fabricated of BaF₂ optical windows with high transmittance of midinfrared light, and the internal reflection plane was confirmed using OCT (IVS-2000, Santec, Komaki, Japan). Figure 2(a) shows the optical system. To visualize the generated reflective surface, pure water containing red fluorescent polymer microspheres (36-3, Thermo Fisher Scientific, Waltham, Massachusetts) was used as a sample. An ultrasonic transducer (PN-10C10N, Japan Probe Co. Ltd., Yokohama, Japan) was attached behind the target, and vibrated

at a frequency of 10 MHz and a voltage of 10 V to generate an ultrasonic standing wave inside the target. The OCT image confirmed that the particles in the water aggregated at the node of the ultrasonic standing wave and formed lines [Fig. 2(c)]. The particles near the boundaries with the optical windows were not trapped by the standing wave and did not aggregate. Because incident light is reflected by a node with a large refractive index difference, the incident light is considered to be reflected 0.05 mm from the wall surface. In this case, the optical path length is the sum of that of the incident light and the reflected light from the reflection plane. We selected a reflectance depth of 0.05 mm, because it provided an optical path length of about 100 μm, which is suitable for midinfrared spectroscopy. To generate a reflection plane at this position, a frequency of 10 MHz is required. Even though the sample is homogeneous and internal reflected light cannot usually be detected, it could be detected from node positions by generating a refractive index difference with an ultrasonic standing wave.

3 Measurement of Glucose in Normal Urine by Midinfrared Spectroscopy

We constructed an optical system for detecting internal reflected light in pure water [Fig. 3(a)]. We used a small graphite light source (EK8620, Helioworks, Santa Rosa, California) with an attached setup for Kohler illumination. To shorten the optical path length, the incident light from the optical system entered through the wall of the target at an angle of about 45 deg. The ultrasonic vibrator was placed on the bottom of the target. We detected internal reflected light using the two-dimensional

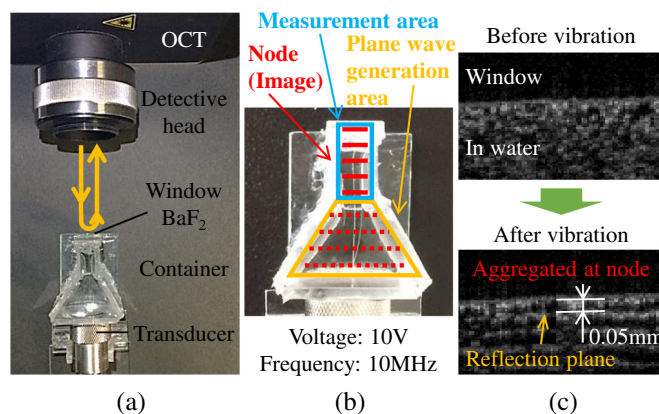


Fig. 2 A reflection plane generated by an ultrasonic standing wave is detected by OCT. (a) Experimental setup, (b) a detailed image of the container, and (c) the results of an experiment.

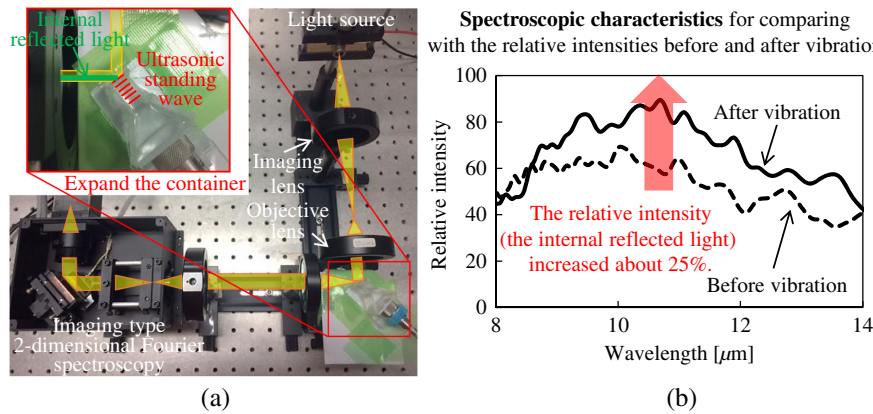


Fig. 3 (a) The optical system for the experiment and (b) comparison of the intensities before and after ultrasonic vibration.

Fourier spectroscopic imager.²⁰ This light was reflected from the reflection plane, which was generated 0.05 mm from the surface by the ultrasonic standing wave using the wall surface as the reflective material. Next, we compared the relative intensities before and after generation of the ultrasonic wave to confirm detection of internal reflected light by our proposed liquid cell. The relative intensities were evaluated for areas of five pixels by five pixels [Fig. 3(b)]. The relative intensity from 8 to 14 μm after ultrasonic vibration was about 25% more than that before ultrasonic vibration. These results confirmed that internal reflected light was detected by our method. The refractive index of the optical window material (BaF_2) is 1.414 at 9 μm .²¹ Thus, the reflectance after vibration was calculated as 8% using Fresnel equations.²² Additionally, using the 25% increase in the relative intensity, the reflectance before vibration was calculated as 2% (25% of 8%). Consequently, the refractive index of water was calculated as 1.1 using the reflectance formula,²³ and the refractive index difference was around 0.3. This value is equivalent to the refractive index when light is reflected on the reflection plane. In future work, we will verify this and determine the theoretical relationship between the reflected light intensity and the ultrasonic standing wave.

Next, a solution of glucose in urine was poured into the container and we measured the glucose absorbance with the optical system using the internal reflected light [Fig. 3(a)]. We spiked the urine with glucose at three concentrations (50, 100, and 200 mg/dL). These concentrations were selected because they are around the level that is considered a positive result

for urine tested with a glucose test strip (100 mg/dL). The relative intensity of the urine after ultrasonic vibration was used as a reference for calculating the absorbance of glucose in urine. We repeated the measurement 30 times and calculated the average. Absorption peaks for glucose were observed at 9.25 and 9.65 μm , respectively [Fig. 4(a)]. The peak at 9.25 μm was not obstructed by other components in the urine [Fig. 4(b)], and we obtained a high correlation coefficient (0.91) for measurement of the glucose concentration in urine using this peak. Therefore, this method is feasible for quantitative measurements of glucose concentrations in urine without a complex setup.

However, the 3σ value calculated from the standard deviation for the 30 measurements at 9.25 μm was about 0.015, and the reproducibility of this method cannot be guaranteed. This could be caused by absorption of midinfrared light by water in the atmosphere, or by fluctuation of the output from the light source. Our proposed method of one-shot Fourier spectroscopy could overcome this problem, because it has high time resolution.²³

4 Conclusions

Our liquid cell, generated by an ultrasonic standing wave in a sample, could be used for realization of smart toilets using midinfrared spectroscopy. In future work, we will study the optimum shape of this liquid cell for installation into smart toilets. Additionally, the stability and repeatability of the liquid cell for urine glucose and protein measurements will be verified by developing a one-shot Fourier spectroscopic imager for use in the midinfrared region.

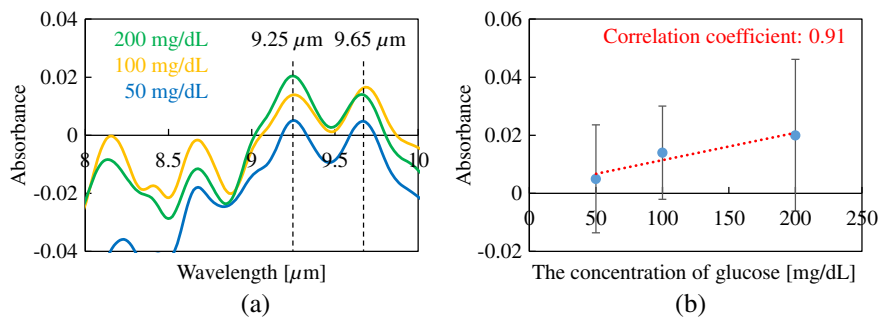


Fig. 4 (a) Absorbance of glucose in urine ($n = 30$) and (b) verification of the measurement accuracy at 9.25 μm .

Disclosures

We declare no conflict of interest.

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