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ABSTRACT

For blood glucose level measurement of dialysis machines, we proposed AAA-battery-size ATR (Attenuated total reflection) Fourier spectroscopy in middle infrared light region. The proposed one-shot Fourier spectroscopic imaging is a near-common path and spatial phase-shift interferometer with high time resolution. Because numerous number of spectral data that is 60 (= camera frame rare e.g. 60[Hz]) multiplied by pixel number could be obtained in 1[sec.], statistical-averaging improvement realize high-accurate spectral measurement. We evaluated the quantitative accuracy of our proposed method for measuring glucose concentration in near-infrared light region with liquid cells. We confirmed that absorbance at 1600[nm] had high correlations with glucose concentrations (correlation coefficient: 0.92). But to measure whole-blood, complex light phenomenon caused from red blood cells, that is scattering and multiple reflection or so, deteriorate spectral data. Thus, we also proposed the ultrasound-assisted spectroscopic imaging that traps particles at standing-wave node. Thus, if ATR prism is oscillated mechanically, anti-node area is generated around evanescent light field on prism surface. By elimination complex light phenomenon of red blood cells, glucose concentration in whole-blood will be quantify with high accuracy. In this report, we successfully trapped red blood cells in normal saline solution with ultrasonic standing wave (frequency: 2[MHz]).

Keywords: Quantitative measurement, Fourier spectroscopy, Spatial phase shift interferometer system, Ultrasound, Blood glucose level, Dialysis machines, Red blood cells, In-situ monitoring

1. INTRODUCTION

We proposed the one-shot Fourier spectroscopic imaging [1] [2]. The proposed method will be developed into AAA-battery size ATR spectroscopy in middle infrared light region. The extremely compact sensor is expected to be applied to blood glucose level measurement for dialysis machines. Patients of diabetic renal disease could not control blood-sugar level well. Thus, during dialysis patients are sometimes prone to hypoglycemia. Therefore, at least alert against low blood sugar will be helpful for patients and nurses. To measure the glucose concentration from light absorbance, absorbance sensitivity of middle infrared lights is very high. But to avoid water absorbance, ATR is inevitable for absorption photometry in mid infrared light region. But to measure whole-blood, red cells scatter illumination lights and deteriorate spectral absorbance. Thus, we also proposed the ultrasound-assisted spectroscopic imaging for separating particle-area at node and liquid-area at anti-node with standing wave [4]. Because particles are trapped into nodes by acoustic radiation pressure, blood glucose can be measured at anti-node area. Anti-node area could be generated around evanescent light field by oscillating ATR prism itself. In this case, blood glucose concentration in whole-blood will be measured quantitatively with high accuracy.

In this report, we evaluated the statistical quantification improvement by one-shot Fourier spectroscopic imaging using glucose solution in liquid cell with near infrared lights. And we demonstrated the feasibility of trapping blood cells in normal saline solution by ultrasound standing wave.

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2. ONE-SHOT FOURIER SPECTROSCOPIC IMAGING

The schematic optical configuration is shown in figure 1. One-shot Fourier spectroscopic imaging is a spatial phase-shift interferometer between objective beams. We install a relative-inclined phase-shifter, what is configured with cuboid and wedge prism(inclination angle: around 1[deg.]), into optical Fourier transform plane. And also we introduce cylindlical lens as imaging lens. Thus, horizontal axix on imaging plane is assigned to spatial phase shift value. And vertical axis on imaging plane is corrresponds to imaging axsis. Rays from single brights points on objective plane are collimated by objective lens. And half flux of collimated objective rays are spatiall phase shifted by wedge prism. Then rays penetrated cuboid prism and wedge prism are spatially interfered in horizontal axis on imaging plane. Thus, interferogram of single bright points is obtained as spatial fringe pattern that is intensity distribution at each pixel in a horizontal pixel arrray. Single bright points on a imaging line form fringe patterns at different coordinate in accrodance with field angles. Spectral characteristics on a imaging line is obtained in one frame image data by 2-dimensional light receiving device. Because the proposed method obtain spectrum as spatial fringe pattern, optical path length could be extremely shortened unlike wavelength dispersive spectrometer. The proposed method will be able to construct as beams size that can be installed into smartphone.

In recent years, low price (less than 300USD) and extremly small (diameter around 1 dime size) 2-dimensional light receiving device became to be commercially avairable products (e.g. Maker: FLIR, Type:FLIR -ONE). And cannned graphite light sources (e.g. Maker:Hawkeye Technologies Size: 2.2×2.2[mm] Output power: 767tipical/1000Max [mm]) could be applied into our Fproposed method. Thus, we had designed AAA-battery-size ATR Fourier spectroscopy in middle infrared light region.

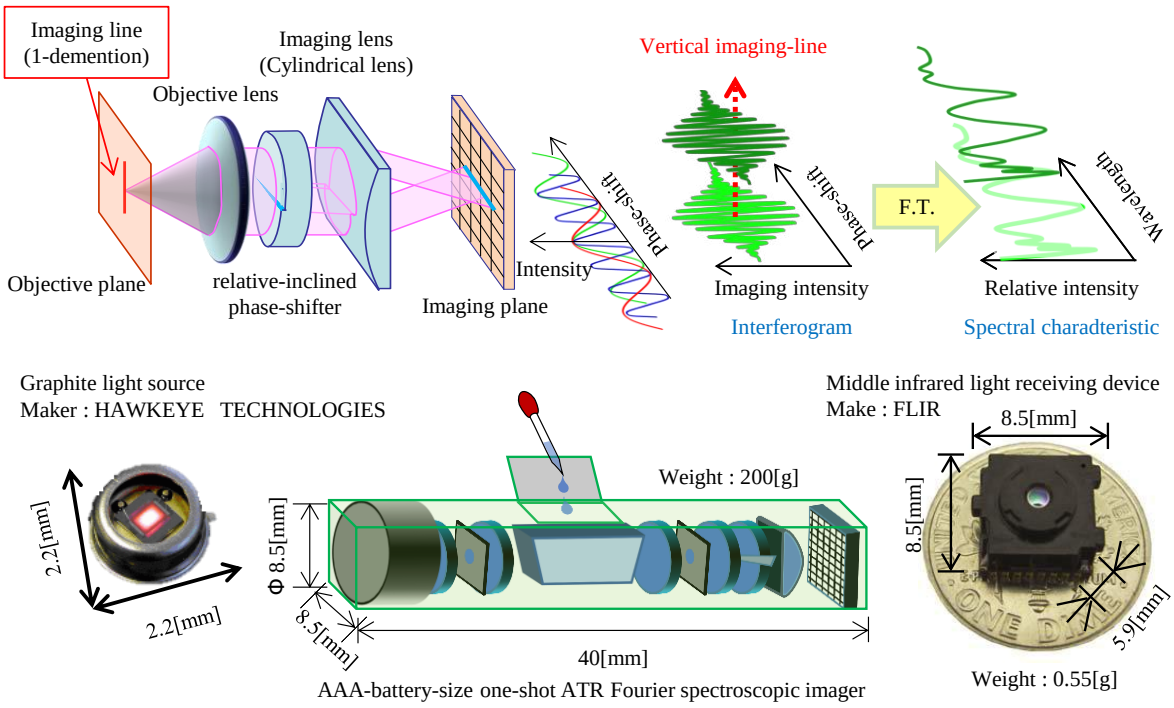
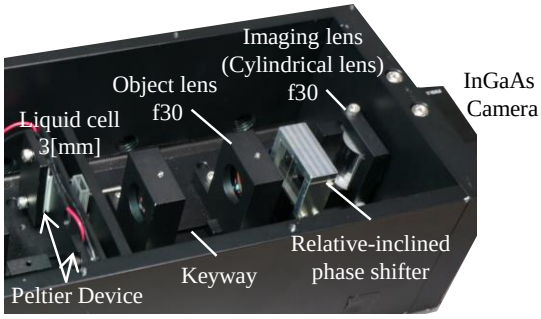


Fig.1 Configuration of AAA-battery-size ATR Fourier spectroscopic apparatus based on one-shot Fourier spectroscopic imager.

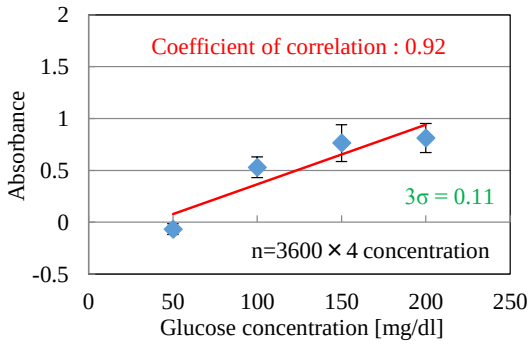
3. EXPERIMENTAL EVALUATION OF STATISTICAL QUANTIFICATION IMPROVEMENT BY ONE-SHOT FOURIER SPECTROSCOPIC IMAGING [3]

As shown in figure 2(a), we constructed the one-shot Fourier spectroscopic apparatus (maximum optical path difference: 382[nm], wavelength resolution: 13[nm]) for evaluating the measurement accuracy of glucose concentration in liquid cells. Temperature of liquid cells were controlled by Peltier devices within 36±0.1[℃] under dried nitrogen purge

environment. Because the proposed method can measure the line distribution of spectroscopic characters with one frame image with high time resolution, we can obtain 60 spectra in 1[sec.] using camera with 60[fps]. For evaluation of the quantitative accuracy, we measured the extremely low glucose concentrations that corresponded to human blood-sugar level. We used 4 kinds concentration of glucose water solution (concentration range: 50[mg/dl]-200[mg/dl]). The super continuum (Maker: Fianium, Type: WhiteLase SC480-2, Wavelength range: 480-2400[nm]) was used as broadband near-infrared light-source. InGaAs camera (Maker: Hamamatsu Photonics K.K., Type: C10633-13, Detective wavelength region: 900[nm]-1700[nm]) was used as 2-dimensional light receiving device. As shown in figure 2(b), we calculated the temporal average of 60 measurement data obtained within 1[sec.]. From this evaluation results, we could discriminate each glucose concentration with correlation coefficient 0.92 and demonstrated the statistical improvement for high accuracy quantitative measurement.



(a) One-shot Fourier spectroscopic apparatus for quantification of glucose concentration in liquid cells



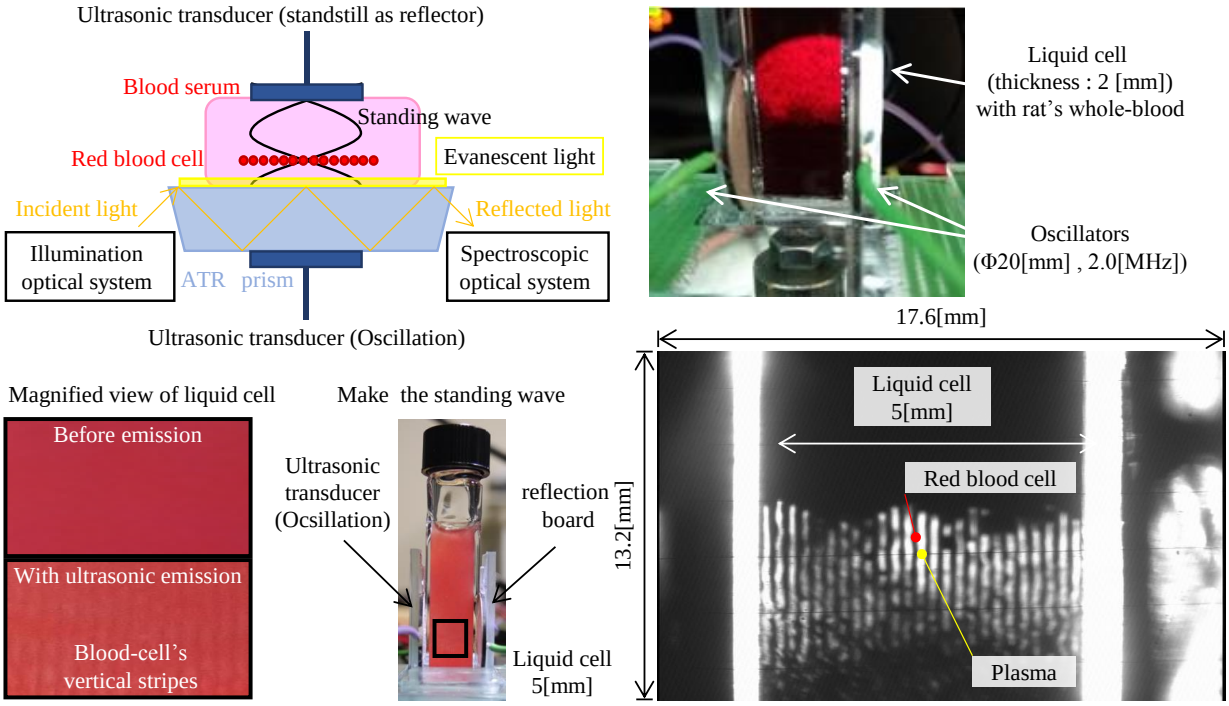
(b) Temporal average of 60 measurement data within 1[sec.]

Fig.2 Experimental results for extremely low glucose concentration solution measured by one-shot Fourier Spectroscopic Imager.

4. EXPERIMENTAL RESULTS OF ULTRASOUND-ASSISTED SPECTROSCOPIC IMAGING OF WHOLE BLOOD

In the case of measuring whole bloods, the light scattering or multiple reflection or absorption caused by red blood cells become the major issue. As shown in figure 3 (a), we proposed the ultrasonic assisted spectroscopy to eliminate complex light-phenomenon of red blood cells. If ultrasonic transducer oscillate ATR prism, standing wave is generated between sound reflector and prism surface. And anti-node is generated around evanescent field on ATR prism surface. Particles like red blood cells are trapped at nodes by acoustic radiation pressure. Thus, at anti-node area we can measure liquid components by eliminating particle components. As shown in right hand side photo of Fig.3 (a), we used liquid cells (thickness: 5[mm]) that is sandwiched between circular transducers (resonance frequency: 2 [MHz]). And we added red blood cells of rat to normal saline solution. We could confirm standing wave (wavelength: 0.7 [mm], applied voltage: 8[V], current: 0.1[A]) and trapping of red blood cells at nodes.

As shown in Figure 3 (b), we demonstrated the feasibility of rat's whole-blood separation in liquid cells (thickness: 2[mm]). We could confirm stripe patterns of agglutinated red blood cells by using two ceramic ultrasonic oscillators (diameter: 20[mm], resonance frequency: 2.0[MHz], Voltage: 22[Vrms]). The sinusoidal wave generated by a function generator (maker: Rigol, type: DG4102) was amplified through a power amplifier (maker: NF, type: HSA 4014). Photograph of Fig.3 (b) was taken by monochromatic change-coupled device (CCD) camera (maker: Sony, type: XC-77, pixel pitch: 8.8×6.6 [mm]). The optical magnification of an observation system was 1/2 and the field of view was 17.6×13.2 [mm]. Then, we were able to detect the transmitted lights through the plasma area of stripe patterns. The estimated interval 0.4[mm] of stripe patterns was almost equivalent to the design value 0.39[mm] because the number of red blood cell aggregation stripe was 25.



(a) Blood-cells trapping at nodes of ultrasonic standing-wave (b) Experimental results of whole-blood separation

Fig.3 Ultrasonic-assisted spectroscopic imaging of eliminating blood cells.

CONCLUSION

For in-situ blood glucose level measurement of dialysis machines, we proposed AAA-battery-size ATR Fourier spectroscopy that is based on one-shot Fourier spectroscopic imaging. We could evaluate statistical quantification improvement of glucose concentration by high time resolution. In addition, we proposed the ultrasound-assisted spectroscopic imaging for whole-blood. We demonstrated the trapping phenomenon of red blood cells at Blood serum nodes.

In the future work, we will combine ultrasound-assisted method and one-shot ATR Fourier spectrometer to evaluate the measurement accuracy of glucose concentration using whole-blood.

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