# Possible correlation between second-order dispersion and glucose concentration investigated by low time-coherence interferometry

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A possible correlation between second-order dispersion and glucose concentration is presented for the first time. The second-order dispersions of three different glucose concentrations: hypoglycemia, normal level, and hyperglycemia are analyzed over the wavelength range from 0.55 to 0.8 $\mu$m by Fourier analysis of the interferogram. The preliminary correlation between second-order dispersion and glucose concentration is investigated by linear fitting the second-order dispersion from 0.65 to 0.75 $\mu$m. This correlation is expected to determine the different glucose concentrations by measuring the second-order dispersion, which can be considered as a potentially noninvasive method to measure glucose concentration in human eye.

*OCIS codes:* 170.1470, 170.3890, 170.0170, 120.3930.

At least 170 million people worldwide suffer from diabetes mellitus in recent years[1]. Frequently self-monitoring of blood glucose concentration is necessary for effective treatment and control of this disease. Currently glucose concentration is measured by puncturing the figure to obtain a drop of blood, which is invasive, unpleasant, inconvenient, and expensive for daily monitoring. Attentions have been drawn to explore noninvasive and cheap techniques for measuring glucose concentration, and considerable progress have been made in the development of noninvasive glucose monitoring techniques[2−4], which include near infrared (NIR) spectroscopy, Raman spectroscopy, photoacoustic spectroscopy, scattering changes, polarization changes, mid-infrared spectroscopy, and optical coherence tomography (COCT)[1]. In this paper, we present another potentially noninvasive method for evaluating glucose concentration.

White light low time-coherence interferometry (LCI) technique allows high sensitivity and accuracy over a wide wavelength range[5,6] for measuring dispersion of various media[7]. Measurement of dispersion can provide some information about various physical properties of the medium such as concentration, pressure, density, stress, and so on. We employed this technique to investigate the glucose dispersions for different glucose concentrations, and obtained preliminary equation correlation between the slope of the second-order dispersion and glucose concentration.

A schematic diagram of the experimental setup is shown in Fig. 1[8]. An inexpensive 100 W, 12 V halogen lamp is used as the white light source. Köhler illumination is employed to collect and collimate the beam before the light enters the interferometer, and the beam diameter is limited by the entrance aperture A2. One arm (sample arm) is placed with a cuvette filled glucose solution and the other arm (reference arm) is placed with the similar cuvette filled water for dispersion compensation. The beam in sample arm is reflected on a retro-reflector mounted on a motor stage that moves back and forth with a constant velocity performing A-scan. The incident light is split, after reflected by two arms, recombined by beam splitter. The interferogram occurs when the path length difference between the two beams matches within the coherent gate. Focusing lens L4 and Silicon photodiode receiver (New Focus Model 2001) are employed for collecting and recording the interferogram over wavelength range 0.5 to 0.9 $\mu$m. He-Ne laser with wavelength of 0.6328 $\mu$m is employed for position correction.

The parameters in our experiments are chosen as[9] $l$=1 mm, $\lambda_0$=0.85 $\mu$m, $\Delta\lambda$=180 nm, power $P$=600 $\mu$W for dispersion measurement. To minimize the change of other physical parameters, such as pressure, density, stress, temperature, and noise, we choose deep night to perform experiment, and each measurement is performed as soon as possible. The temperature is (27±0.5)°C. A direct current (DC) controller C-842 that drives a motor stage with a constant velocity controls the path length in real time. A beam from He-Ne laser that is parallel carefully with white light is recorded for actually path length correction. The same experiment is repeated twenty times, where each measurement needs two seconds, and twenty data sets are recorded from the measurement. Considering of the weak glucose dispersion, and the human eye length (from cornea to retina) of about 20 mm, we select the path length as $l = (20 \pm 6.467 \times 10^{-4})$ mm,

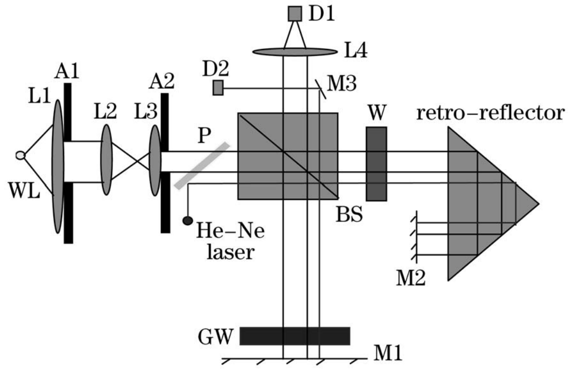


Fig. 1. Schematic diagram of Michelson interferometer with Köhler illumination. WL: white light; A1, A2: stop and entrance apertures; L: lens; P: pellide beam splitter (10:90); D: detectors; M: plane mirrors; W: water; GW: glucose solution.

1671-7694/2005/0s0091-03 http://www.col.org.cn

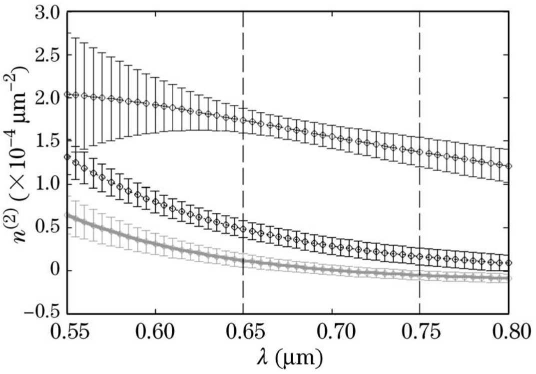


Fig. 2. The second order dispersions of different glucose concentrations. Dashed line: hyperglycemia; dotted line :normal level; solid line: hypoglycemia.

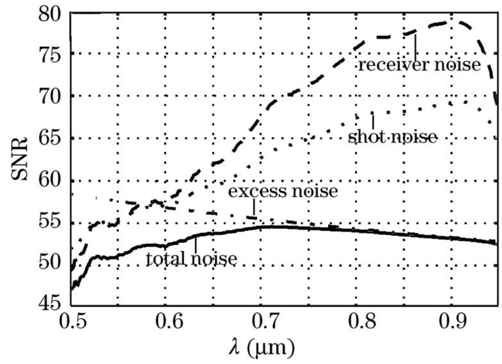


Fig. 3. SNR of interferogram as a function of wavelength for reflectivities of the sample and reference arms with $R_s$=0.8 and $R_r$=0.53, respectively. Dashed line: receiver noise; dotted line: shot noise; dashed and dotted line: excess noise; solid line: total noise.

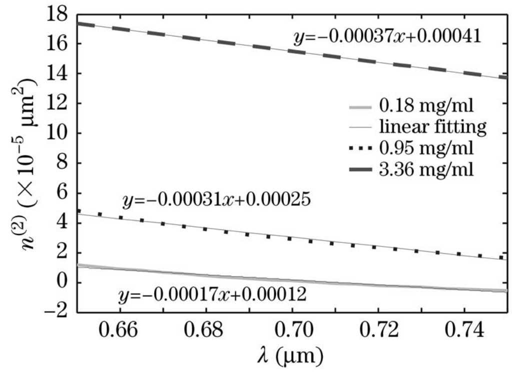


Fig. 4. Linear fitting of second-order dispersion against wavelength for different glucose concentrations.

and the experiment is repeated for different glucose concentration solutions. It is worth noting that for zero glucose concentration, the two arms are arranged as: water + glass & water + glass, and for the non-zero glucose concentration, two arms arranged as: water + glass & glucose solution + glass. Corresponding second-order dispersion and its standard deviation are illuminated in Fig. 2, where solid, dotted, and dashed lines present three different glucose concentrations: hypoglycemia, normal level, and hyperglycemia, respectively.

The error bar consists of systematic and statistical parts. On one hand, systematic error bar comes from detector responsivity and spectrum unstability, which is regular, on the other hand, statistical error bar is irregularly scattered. It is evidently seen from Fig. 2 that different second order dispersions are associated with different concentrations: the higher glucose concentration level is, the more second order dispersion is. As a consequence, measuring the second order dispersion, one is able to determine glucose concentration. The correlation between second-order dispersion and glucose concentration will be deduced from our measurement.

From Fig. 2, besides the dependency of dispersion on glucose concentration, for normal and lower concentration level, standard deviation decreases and then increases as wavelength decreases. Signal-to-noise ratio (SNR) of the interferogram[10−12], which is deduced from system, including shot noise, excess noise, receiver noise, is plotted as a function of wavelength in Fig. 3 for the actual reflectivities of the sample and reference arms with $R_s$=0.8 and $R_r$=0.53, respectively. Since SNR is calculated from interferometer's system (time domain), it can be used to estimate the error bar roughly. Error bar (standard deviation) comes from spectrum phase, which includes system error, statistic error, and calculation error. The SNR can be used to analyze qualitatively the error bar. The shorter and longer wavelengths exhibit lower SNR corresponding to bigger error bar, as clearly shown in Fig. 3. SNR reaches its maximal values over 0.65−0.82 $\mu$m. However, the second order dispersion is very small for longer wavelength because of the dependency of wavelength[9]. The error bar is bigger for higher concentration level than lower level, which is attributed to glucose molecule scattering and moving within the glucose solution because the size of glucose molecule is bigger than that of water, but smaller than wavelength. The wavelength range over 0.65−0.75 $\mu$m is selected (see Figs. 2 and 4) to analyze the correlation between second-order dispersion and glucose concentration level because of their small error bar, high SNR, and high quantumn responsivity of photodetector over this wavelength range.

Three different concentration levels, hypoglycemia, normal level, and hyperglycemia, are taken from the above container, and measured as: $C_{0.2}$=0.18±0.01 mg/ml (expected 0.2 mg/ml), $C_1$=0.95±0.02 mg/ml (expected 1.0 mg/ml), and $C_{3.4}$=3.36±0.04 mg/ml (expected 5.0 mg/ml), at pH values of 7.38±0.02, 7.37±0.02, 7.38±0.02, respectively, by glucometer in Austrian General Hospital.

Figure 5 displays the measured curve and fitted linear line with its fitting linear equation, and the fitting parameters as well. It is obviously seen that the slopes of different concentrations' curves are 1.7, 3.1, and 3.7 for three different glucose levels. Furthermore, zero glucose concentration has zero dispersion, the second order dispersion should be zero, this value is added into Fig. 5.

Further fitting polynomial to data, one can see the correlation between the slope of second-order dispersion ($sk_i$) and glucose concentration ($C_i$) is exhibited in Fig. 5. The correlation equation is

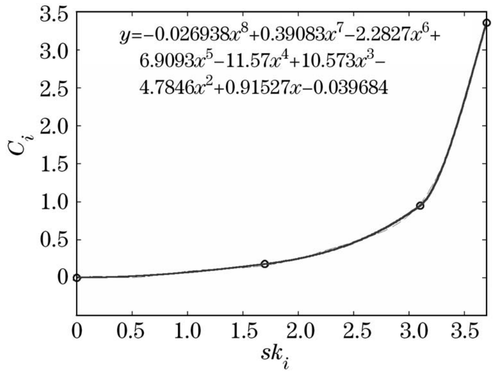


Fig. 5. The correlation between the slope of second-order dispersion ($sk_i$) and glucose concentration ($C_i$).

$$\begin{aligned} C_i &= -0.026938sk_i^8 + 0.39083sk_i^7 - 2.2827sk_i^6 \\ &+6.9093sk_i^5 + 11.57sk_i^4 + 10.573sk_i^3 \\ &-4.7846sk_i^2 + 0.91527sk_i - 0.039684. \end{aligned} \quad (1)$$

For any measured $sk_i$, one can determine the glucose level using Eq. (1). It is worth mentioning this correlation is firstly deduced from our experimental data between 0.2 and 3.4 mg/ml over the wavelength range from 0.65 to 0.75 $\mu$m, and it should be continued to perform further experiments over wider concentration levels range for improving and enriching this correlation in future.

In general, a preliminary correlation between the slope of the second-order dispersion and glucose concentration level is investigated for the first time. Three different glucose concentrations, hypoglycemia, normal level, and hyperglycemia are analyzed, and correlation equations for glucose concentration levels are derived from our investigation. In the future, OCT technique can measure the path length of human eye precisely if another superluminescent diode (SLD) light source with different wavelengths is introduced by use of dichroic reflector in this system. It is possible to detect the human eye's length and glucose concentration with only one scan in one system *in vivo*, and this approach can be expected for further noninvasive glucose concentration measurement in human eye *in vivo*.

This research is sponsored by the National Natural Science Foundation of China (No. 30300080), Beijing Natural Sciences Foundation (No. 4042023), and the Scientific Research Foundation for the Returned Overseas Chinese Scholars, State Education Ministry. J. liu's e-mail address is juanliu@center.njtu.edu.cn.

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