

High SNR Glucose Monitoring using a SWIR Super-Continuum Light Source

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Abstract: We measure glucose solutions down to 1mg/dl based on the C-H combinational bands using a short-wave infrared super-continuum (SWIR-SC) laser. We estimate that the SWIR-SC increases the measurement system SNR by >50x compared with lamps.

OCIS codes: (300.6340) Spectroscopy, infrared; (300.6360) Spectroscopy, laser; (190.4370) Nonlinear optics, fibers

We demonstrate that low concentration glucose solutions down to 1mg/dl can be measured using an all fiber integrated short-wave infrared super-continuum (SWIR-SC) laser as the light source in a balanced arm spectroscopy system. Measuring glucose concentrations in aqueous solutions down to 1mg/dl is proposed as the first step in a “test of technologies” towards a viable non-invasive glucose monitoring approach in Ref [1]. To our knowledge, no other non-invasive technique has been able to detect glucose in aqueous solution at this concentration, and almost all infrared spectroscopic techniques to date have relied on tungsten or halogen lamps. We estimate that our SWIR-SC laser improves the system SNR by at least 50 times compared to lamps due to the high brightness reaching the detector without saturation, even after passing through a highly absorbed background such as water. In addition, the glucose combinational bands from ~2000nm to ~2400nm are used, since they fall in water absorption minimum valleys without interference from hemoglobin features (e.g., FTIR spectra in Fig.1). Therefore, a SWIR-SC could be a key enabling technology for non-invasive glucose monitoring.

The spectroscopy system used for the measurements is a balanced arm spectroscopy system with a SC laser as the light source shown (Fig. 2). The SWIR-SC is an all-fiber integrated SC laser covering the 1500~2400nm wavelength range with an output up to 5W. The laser is a diode laser followed by two-stages of fiber amplifier and a nonlinear fiber for spectral broadening, as further detailed in Ref. [2].

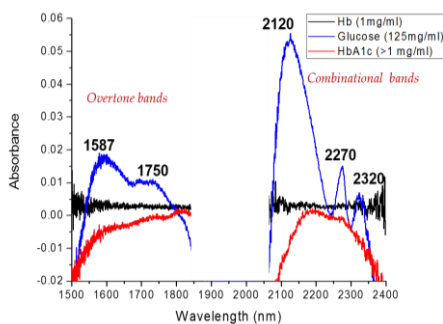


Fig. 1 Glucose absorption in first overtone and combinational bands

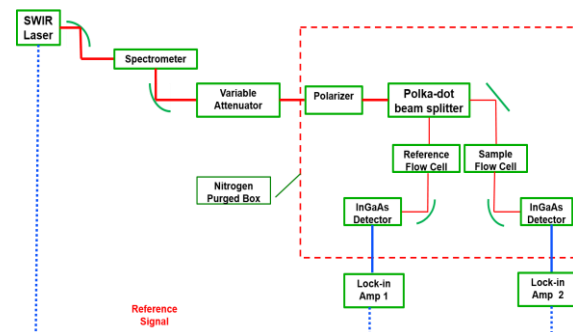


Fig.2 Schematic diagram of SC spectroscopy system

The system in Fig. 2 is designed to achieve the high repeatability and SNR required for detecting 1mg/dl glucose solution. The light from the SWIR-SC enters a balanced arm sub-system followed by a detection sub-system. The wavelength of light is selected by sending the SWIR-SC output to a monochromator with ~5nm output bandwidth. Only ~250mW optical power is sent into the spectrometer and ~50mW after the attenuator in the experiments to prevent detector saturation. The balanced arm sub-system comprises a broadband beam splitter and two flow cells used for sample and reference solutions, respectively. A matched pair of InGaAs detectors are used for light detection, and data is collected through two lock-in amplifiers synchronized to the laser output. The SNR at highest intensity is measured to be ~47dB, and the repeatability of the system is within -40dB, as tested by comparing the spectral difference between two consecutive background measurements (shown in Fig.3).

A series of measurements are done on glucose aqueous solutions of different concentrations. The concentrations used in this test are 100mg/dl, 50mg/dl, 25mg/dl, 10mg/dl, 5mg/dl, 2.5mg/dl and 1mg/dl. The SWIR spectrums are taken from 2000nm to 2400nm with a 5nm step. Five spectrums are recorded and averaged at each concentration. At the beginning of the experiment, background spectrums are taken by injecting deionized (DI) water into both

sample and reference cells. During the experiment, glucose solutions, starting with the 1mg/dl solution, are injected into the sample cell while DI water is injected into the reference cell. The time taken for one measurement is ~10min due to the slow mechanical scanning rate of the monochromator. The acquired data is processed by standard spectral processing techniques including smoothing and baseline correction. Amplitude drift between measurements is corrected by aligning spectrum to a known-absorption valley at 2240nm.

Exemplary glucose spectrums taken at different concentrations are shown in Fig. 4. Not shown here is the 2.5mg/dl and 1mg/dl spectrum, since their amplitude is too low to be shown in this scale. The first (2120nm) and second (2280nm) absorption peaks are very distinct, although the spectrum features after 2300nm show background fluctuations caused by temperature dependence of water absorption. Also, we believe the etalon effects in the spectrum may be due to reflections in the detector cover glass.

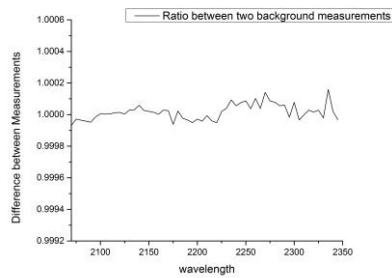


Fig.3 Difference between two background measurements

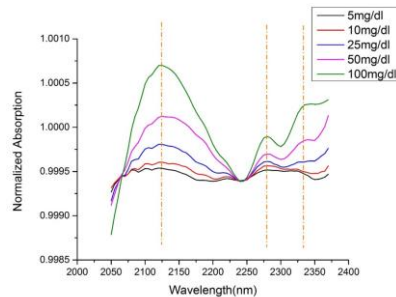


Fig.4 Measured glucose spectra of different concentrations

To validate that our system is properly measuring glucose, we verify that the absorption at the first two absorption peaks are linearly proportional to glucose concentration, as predicted by Beer's Law. A linear fitting analysis was conducted on the peak value of the first and second glucose absorption peaks of lower concentration solutions (1-50mg/dl), and the highly linear relationship (Fig.5) between concentration and absorption confirms that we are measuring glucose. Also note that at the lower concentrations the linearity is maintained although the absorption becomes negative because of the large water absorption background [3].

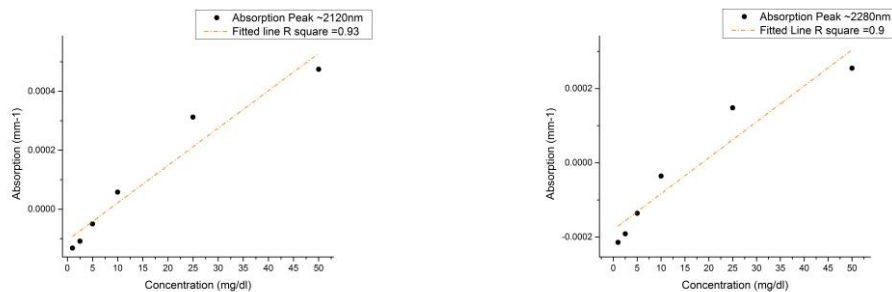


Fig.5 (a). Linear relationship between absorptivity and glucose solution concentration at 2120nm.
(b) Linear relationship between absorptivity and glucose solution concentration at 2280nm.

We show that infrared spectroscopy of glucose can be done in the combination bands, where water absorption has a local minimum and hemoglobin is featureless. With the high brightness provided by the SWIR-SC, it is possible to detect glucose solution absorption down to 1mg/dl, which corresponds to absorption changes in the 4th to 5th decimal place. A properly balanced detection setup is necessary, since at such low signal level any environmental fluctuation such as temperature or humidity could distort the measured signal (c.f. Fig. 4). The SNR upper limit is set by the maximum SNR of the detection electronics and detector saturation power, not by the input optical power. Our estimate of better than 50x improvement (>47dB) by using the SWIR-SC compared with a halogen or tungsten lamp is based on considering not only the laser power but also the detector saturation.

In summary, we measure glucose concentrations down 1mg/dl in aqueous solution in a balanced arm spectroscopy system using a SWIR-SC, which improves the SNR of the set-up by >50x compared to lamps. We also show linearity of the absorption strength of the C-H combination band features with glucose concentration.

References

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