Towards Fiber-Optic Raman Spectroscopy for Glucose Sensing

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Abstract: We demonstrate a multimode optical fiber sensor for spectroscopic Raman measurements of glucose concentration for the application in intraperitoneal glucose detection in diabetic patients. A regression model with a RMSEC of 2.2 mM was obtained.

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1. Introduction

Both the incidence and prevalence of diabetes mellitus type 1 and 2 are increasing worldwide [1], therefore a reliable and convenient way of continuous glucose monitoring (CGM) is required. The existing standard for glucose measurements is based on subcutaneous (SC) sensing, but this method still faces challenges due to slow dynamics and time delays, as well as poor robustness caused by local tissue changes such as mechanical pressure and temperature fluctuations [2]. However, intraperitoneal (IP) glucose measurements can offer faster dynamics and are less predisposed to mechanical disturbances [3]. Since the IP CGM requires *in vivo* measurements using a small diameter probe in a well-controlled location, a single optical fiber (OF) sensor is proposed in this work.

OF sensors have gained large interest in the last two decades, especially in environmental and bio-sensing applications, as a result of many important advantages, such as light weight, small size, potential for high sensitivity, and immunity to electromagnetic fields [4]. More importantly, OF sensors have unique properties of performing measurements at inaccessible locations. Moreover, OF sensors based on Raman spectroscopy that provides fingerprints of specific molecules without the need for labeling elements, have potential for *in vivo* remote and real-time detection in biomedical diagnostics. Glucose detection by Raman spectroscopy based on a photonic crystal fiber has been previously presented [5]. However, it required an infiltration of the investigated liquid into the 6 cm fiber core extending the time between two successive measurements.

In this presentation, we report a multimode (MM) OF sensor based on Raman scattering in an optrode configuration where the same fiber is used for the excitation and collection of the Raman shifted radiation. The application of the proposed sensor for IP glucose concentration monitoring will be discussed. This work provides a basis for further development of OF based Raman spectroscopy glucose sensors.

2. Experimental

A MM optical fiber was used with 105 μm core - and 125 μm cladding diameters, respectively. The fiber was mounted under the Renishaw inVia Raman Microscope system, so that the light coupling and collection of the Raman signal were conducted through the same end of the MM fiber, while the second end was immersed in studied water-glucose solutions (Fig.1). The measurements were taken with 10 s scanning time and 20 acquisitions using an excitation laser wavelength of 785 nm at 300 mW power. Different concentrations of D-(+)-glucose in aqueous solutions in the range of 0 - 1110 mM were measured over the course of one week.

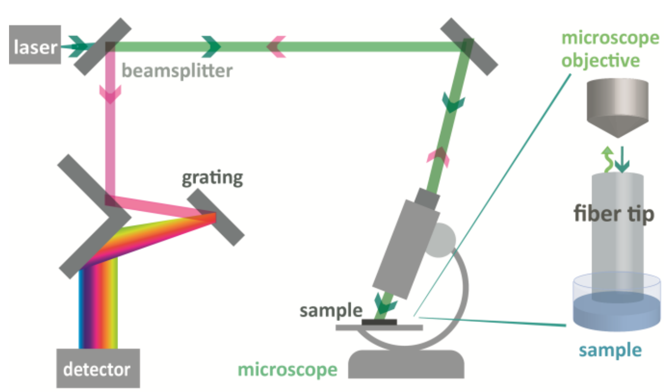
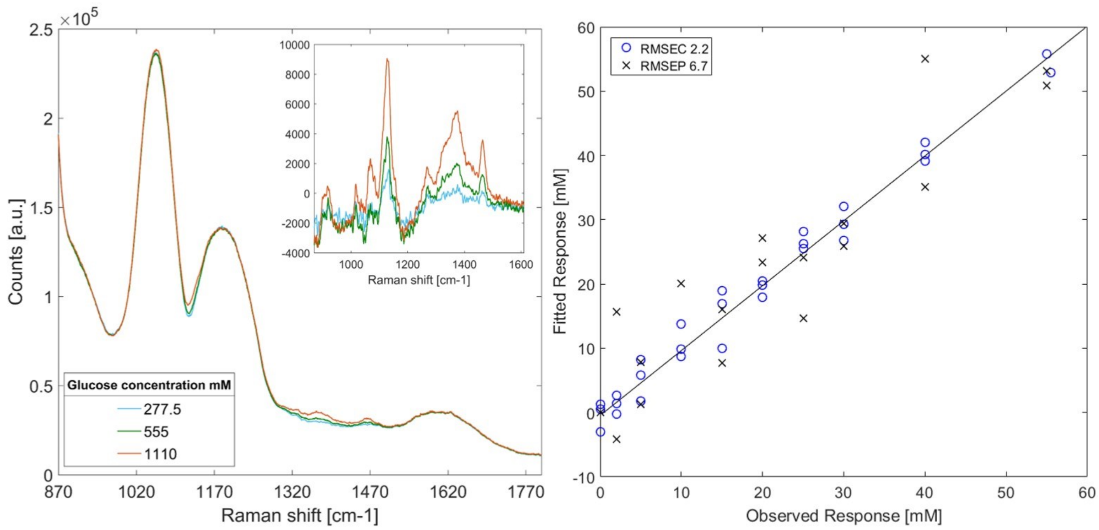


Fig. 1 Schematic of Raman spectroscopic measurement setup with the MM fiber.

3. Results

The measured Raman spectra show an increase in relative intensity as a function of glucose concentration (Fig. 2a), showing linear correlation in the measured concentration range. For the measured Raman signals, a regression model was found using a partial least squares regression (PLSR) algorithm, 36 measurements in the range of 0-110mM were used for calibration and 20 measurements (range: 0-55mM) from two different days were reserved for model validation. One measurement in the calibration and one in the validation sets displayed a different scattering profile and was discarded as an instrumental error. All data was first smoothed using 9-points moving average before Extended Multiplicative Scattering Correction (EMSC) was applied, with the average of the calibration spectra as the reference [6]. A six-component model was chosen based on cross-calibration (leave 2 out) of the calibration set. A baseline shift of the validation set was corrected for a blank sample for each day. The regression model yielded a root mean square error (RMSE) of calibration of 2.2 mM and a corresponding RMSE of prediction of 6.7 mM (Fig. 2b).



(a) (b)

Fig. 2 a) Raman spectra of glucose in aqueous solutions for varying glucose concentration (Inset: background subtracted Raman spectra); b) Measured vs predicted glucose concentration obtained with the PLSR model.

4. Conclusions

In conclusion, we report a MM fiber sensor based on Raman scattering for glucose measurements in aqueous solution. The results demonstrate a possibility of applying the proposed sensor for glucose detection. Future work will focus on further improving the sensitivity by using a surface enhanced Raman scattering fiber tip.

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