2014 CMBEC37 Conference
Vancouver, BC
May 21 – 23, 2014

Optical Glucose Monitoring Sensor

Sahba Talebi Fard†, Ezra Kwok‡, Lukas Chrostowski†

† Department of Electrical and Computer Engineering
University of British Columbia
sahbat@ece.ubc.ca, lukasc@ece.ubc.ca

‡Department of Chemical and Biological Engineering
University of British Columbia
ezra@chbe.ubc.ca

INTRODUCTION

Diabetes Mellitus, being a common chronic disease, and characterized by the inability of the body to control blood glucose concentrations, has become a public health issue.

Currently, most of the common and FDA approved devices are enzyme-based; and a reasonable control requires at least four daily finger-pricks to determine the subsequent insulin injections. Continuous Glucose Monitoring (CGM) improves patient health and their quality of life by stabilizing the glucose levels. Optical methods are one of the painless and promising methods that can be used for blood glucose predictions and establish a reliable CGM.

Our goal is to investigate a novel optical system for accurate glucose predictions. In our group we have investigated absorption spectroscopy using both broadband white light as well as a few low power lasers, Vertical Cavity Surface Emitting Lasers (VCSELs). Using only two VCSELs that have tunable wavelength range of 7nm, along with multivariate methods for preprocessing and model calibrations, we were able to predict concentrations of glucose in buffer solutions, and blood serum with RMSEP of about 1mM and 2mM respectively [1,2]; this means our prediction model's goodness of fit (r^2 value) was 0.997, 0.995 respectively.

We are currently investigating Evanescent Field (EF) sensors [3,4], more specifically silicon-on-insulator (SOI)-based resonator sensors. These SOI sensors, being fabricated in well-developed foundry services, have the potential to be integrated with CMOS circuitry for integration of system on the same chip. The EF sensors operation is based on detecting changes in the refractive index of the cladding medium (which in this case is various concentrations of aqueous solutions of glucose). The EF resonator sensors have shown promises for both surface and bulk sensing.

In this paper we discuss these two optical methods (Absorption Spectroscopy and Evanescent Field sensing) and their suitability as a potential optical sensing method for continuous glucose monitoring.

VERTICAL CAVITY SURFACE EMITTING LASERS (VCSELS) FOR GLUCOSE SPECTROSCOPY

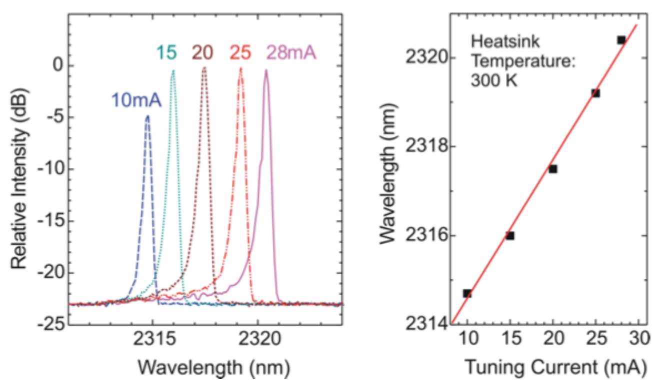

Figure 1: Current dependent optical output spectra of the 2.3 µm LW- VCSEL, and wavelength shift with respect to bias current, at 300K, with the tuning slope of 0.3 nm/mA. The thermal tunability is 0.1 nm/◦C [5].

Semiconductor diode lasers are unique light sources with excellent spectral and beam properties. VCSELs are a type of semiconductor lasers that are attractive for implantable biomedical applications due to their low-cost, small size, array operation, low power consumption, and a circular beam pattern. For spectroscopy application, a range of wavelengths is required. This can be achieved through thermally tuning VCSELs by changing their supplied bias current that results in wavelength change. Figure 1 shows optical spectra of the VCSEL for various bias currents. It shows that this VCSEL can achieve an emission wavelength of 2315 nm, and it can be tuned over 5.6 nm if the driving current is changed from 10 to 28 mA [5].

GLUCOSE PREDICTIONS WITH ABSORPTION SPECTROSCOPY USING VCSELS

The feasibility of using a number of narrow wavelength intervals (~7 nm wide) to predict glucose concentration in aqueous solutions has been demonstrated [1,2,5]. This has been shown by experiments using both white light and VCSELs as well as simulations. Experiments with white light in overtone region, in addition to demonstrating the feasibility of predicting glucose concentration using wavelength intervals, have shown that increasing the number of these intervals improves accuracy up to a point after which the addition of more intervals would not improve the accuracy significantly (figure 2).

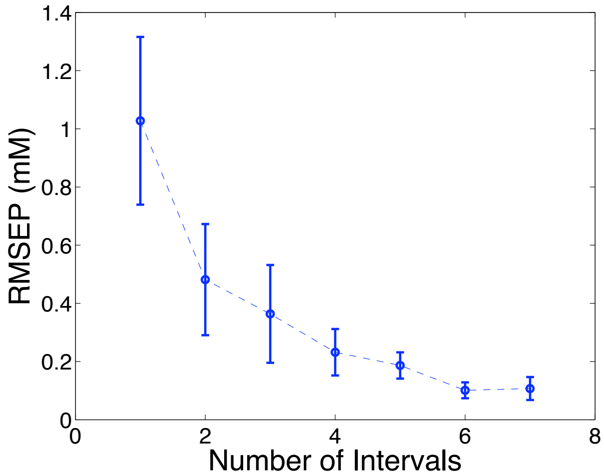

Figure 2. Error (RMSEP) vs. number of wavelength intervals used in model prediction. For example, using two wavelength segments of 7nm, as compared to using one, reduced the error from about 1 to 0.5 mM [1].

An optical glucose sensor based on VCSELs together with data preprocessing and the PLS regression techniques was developed and tested. Summary of the results is presented in figure 3. The RMSEP prediction error was in the clinically relevant range (1.19 mM for a single VCSEL, and 0.77 mM for two VCSELs). These results confirm that this method is a promising method for the development of real-time optical glucose monitors. [2]

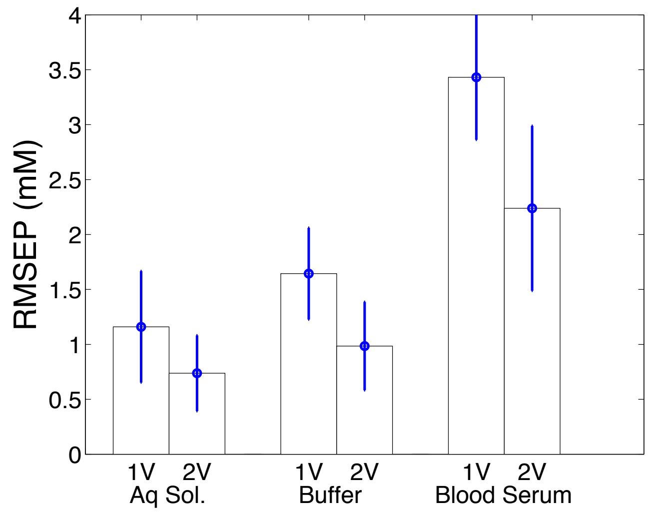

Figure 3: Average prediction error using absorption spectra collected with one VCSEL vs. two VCSELs in various solutions (aqueous, physiological buffer, and blood serum). 1V means absorption spectra from one VCSEL are used; and 2V means absorption spectra of two VCSELs are used [1, 2].

GLUCOSE PREDICTIONS USING EVANESCENT FIELD SENSOR

Evanescent Field (EF) sensors have attracted many researchers for biological sensing applications [1, 4, 6, 7, 8]. These sensors are based on the interaction of the evanescent tail of the guided mode in the waveguide with the analyte in the cladding medium, which as a result changes the effective index of the propagating mode in the waveguide. These optical sensors are one of the promising methods for label-free detection and real-time monitoring. Among the EF optical sensors, resonators have demonstrated strong promises and feasibility in developing on-chip biosensors with small footprint and high sensitivities due to their longer interactions with the solution surrounding the sensor. Figure 4 shows SEM images of some of these devices developed in our group.

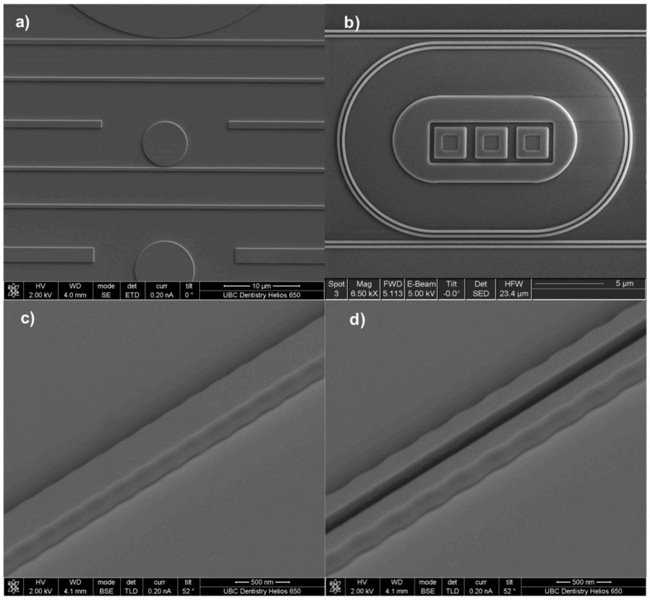

Figure 4: SEM images of some of the EF resonator sensors designed and fabricated in our group [3]. a) disk resonator, b) slot ring resonator, c) Bragg grating, d) slot Bragg grating. [3]

The sensing mechanism of these optical resonator sensors is based on the interaction of the evanescent tail of the propagating optical mode in the sensor with the surrounding solutions. A change in the concentration of the bulk solution surrounding the sensor changes the effective refractive index of the propagating mode, resulting in measurable changes in the optical characteristics of the sensor that can be easily quantified. Therefore, these optical sensors show promise for real-time monitoring.

One type of these sensors (a ring resonator) was tested with solutions of glucose, from which a prediction model was created to predict glucose concentrations. Figure 5 shows the results of using this EF sensor to predict glucose concentrations in aqueous solutions. An RMSEP of about 3.8 mM was achieved with this sensor.

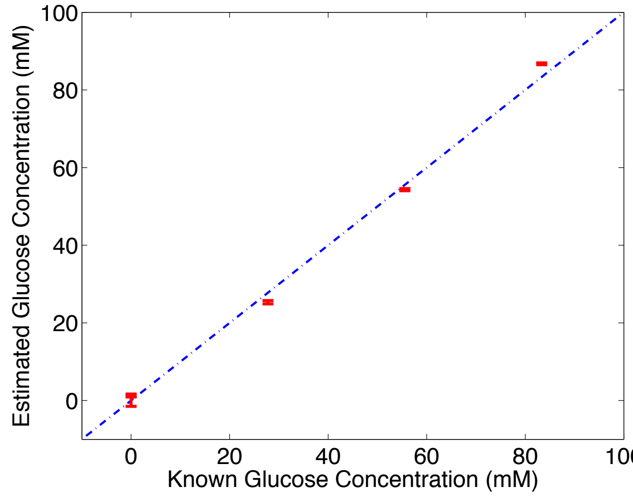

Figure 5: Prediction results of glucose concentrations using EF sensor with a simple linear model. The dashed line shows where estimated concentrations match known concentrations. Each error bar summarizes results of ten measurements.

DISCUSSION AND CONCLUSION

Absorption Spectroscopy together with multivariate data analysis and modeling resulted in clinically required accuracy of +/-1mM. However, this method requires larger optical path in the solution (beer's law) due to small abruption peak of glucose compared to water. In addition, integration of such a sensor with electronics on the same chip is challenging. On the other hand, EF sensors and specifically resonators fabricate in CMOS compatible processes have the potential of being integrated with electronics for the purpose of developing lab-on-chip. EF sensors have advantages such as immunity to EMI, and low cost in case of mass fabrication, being fabricated with CMOS-compatible silicon-on-insulator (SOI). Sensors with small footprint are specifically desirable for biological applications, as it would imply small amount of sample required. SOI-based sensors will allow efficient development of biosensors to be integrated with on-chip detectors, serving towards the purpose of implementing lab-on-chip (LoC).

REFERENCES:

[1] Sahba Talebi Fard, Werner Hofmann, Pouria Talebi Fard, Ezra Kwok, Markus-Christian Amann, and Lukas Chrostowski. Optical glucose monitoring using vertical cavity surface emitting lasers (VCSELs). Proceedings of SPIE, volume 7397, page 739704, 2009.

[2] Sahba Talebi Fard, Lukas Chrostowski, Ezra Kwok, and M-C Amann. Chemometric approach for improving VCSEL-based glucose predictions, IEEE Transactions on Biomedical Engineering, 57(3): 578–585, 2010.

[3] Sahba TalebiFard, Samantha M. Grist, Valentina Donzella, Shon A. Schmidt, Jonas Flueckiger, Xu Wang, Wei Shi, Andrew Millspaugh, Mitchell Webb, Daniel M. Ratner, Karen C. Cheung, and Lukas Chrostowski. Label-free silicon photonic biosensors for use in clinical diagnostics. Proc. SPIE, Silicon Photonics VIII, 8629:862909–14, 02/2013 2013.

[4] Lukas Chrostowski, Samantha Grist, Jonas Flueckiger, Wei Shi, Xu Wang, Eric Ouellet, Han Yun, Mitch Webb, Ben Nie, Zhen Liang, Karen C. Cheung, Shon A. Schmidt, Daniel M. Ratner, and Nicolas A. F. Jaeger. Silicon photonic resonator sensors and devices. Proceedings of SPIE, 8236(1):823620–823620–16, February 2012.

[5] S. Talebi Fard, W. Hofmann, P. TalebiFard, G. B Bohm, M. Ortsiefer, E. Kwok, M.-C. Amann, and L. Chrostowski, "Optical absorption glucose measurements using 2.3 μ m vertical cavity semiconductor lasers," IEEE Photonics Technology Letters, vol. 20, no. 11, pp. 930–932, 06 2008.

[6] A. Densmore, M. Vachon, D.-X. Xu, S. Janz, R. Ma, Y.-H. Li, G. Lopinski, A. Delaˆge, J. Lapointe, C. Luebbert et al., "Silicon photonic wire biosensor array for multiplexed, real-time and label-free molecular detection," Optics letters, vol. 34, no. 23, pp. 3598–3600, 2009.

[7] M. Iqbal, M. A. Gleeson, B. Spaugh, F. Tybor, W. G. Gunn, M. Hochberg, T. Baehr-Jones, R. C. Bailey, and L. C. Gunn, "Label-free biosensor arrays based on silicon ring resonators and high- speed optical scanning instrumentation," Selected Topics in Quantum Electronics, IEEE Journal of, vol. 16, no. 3, pp. 654–661, 2010.

[8] M. S. Luchansky, A. L. Washburn, T. A. Martin, M. Iqbal, L. C. Gunn, and R. C. Bailey, "Characterization of the evanescent field profile and bound mass sensitivity of a label-free silicon photonic microring resonator biosensing platform," Biosensors and Bioelectronics, vol. 26, no. 4, pp. 1283–1291, 2010.