Investigation of glucose diffusion using an optofluidic silicon chip

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We present a new method to study the diffusion of glucose with an opto-fluidic chip. A silicon-on-insulator chip comprising a series of micro-ring resonators is combined with micro-fluidics in poly(dimethylsiloxane) (PDMS). The ring resonators exhibit a shift in resonance wavelength depending on the applied glucose concentration. Based on this effect, the micro-rings are employed as glucose sensors to monitor how the glucose concentration in the microfluidic channels changes due to diffusion. The obtained concentration profiles are compared with diffusion simulations. The good agreement indicates that the opto-fluidic chip is a valuable platform to study glucose diffusion in a variety of settings.

Introduction

Glucose plays an important role in many physiological processes. Especially faulty blood glucose levels have significant impact on the human health. Diabetes patients e.g. need external regulation of their blood glucose level through insuline injections. However, before every injection, the exact blood glucose level needs to be determined. To achieve this, we are developing an implantable glucose sensor based on evanescent near-infrared absorption spectroscopy. The sensing method takes advantage of the unique absorption spectrum of glucose in the near-infrared. The core of our implant is a miniature near-infrared spectrometer, embedded in a biocompatible polymer to minimize body reactions. The implant has a small cavity that will be filled with interstitial fluid, which is extracellular fluid that bathes most tissues. Based on the spectrum of this small amount of fluid, we will determine the glucose level. Generally, the glucose concentration in interstitial fluid has a close relation with the blood glucose level thanks to the omnipresent blood capillaries. Therefore, the glucose level in interstitial fluid is clinically relevant. However, the cavity in our implantable sensor cannot be filled with blood capillaries due to its shape and dimensions. Glucose molecules can only reach this cavity by diffusion. This setting led us to explore diffusion of the small glucose molecule in water in micro-fluidic channels. Glucose diffusion measurements are performed with an opto-fluidic chip that combines a silicon-on-insulator (SOI) chip with micro-fluidics in poly(dimethylsiloxane)(PDMS). The SOI chip comprises a set of micro-ring resonators that monitor, both in time and space, how the glucose concentration evolves due to diffusion in a microfluidic channel. The obtained measurements are compared with simulations with the commercially available software ANSYS Fluent®. Good agreement was found, indicating that this opto-fluidic chip is a valuable test platform for diffusion studies of small molecules in

micro-fluidic channels. The remainder of this paper is structured as follows: First, we discuss the design and operating principle of the opto-fluidic chip. Secondly, we elaborate on the measurement set-up. We then present the results and discussion to finalize with a conclusion and future outlook.

Design and fabrication of the opto-fluidic chip

The microfluidics are fabricated in poly(dimethylsiloxane) (PDMS) (Sylgard ®184, Dow Corning Corporation) using soft lithography [1]. The fluidic channels are 200 μm wide and 50 μm high. It contains one main channel that connects the inlet with the outlet and a diffusion channel that is a perpendicular branch of the main channel. This diffusion channel is open on one side for glucose to enter, but is closed on the other side so as to avoid flow. The microfluidics design is shown in figure 1(a). Both the silicon-on-insulator chip and PDMS are given a short oxygen-plasma treatment before applying direct bonding with a flip-chip machine.
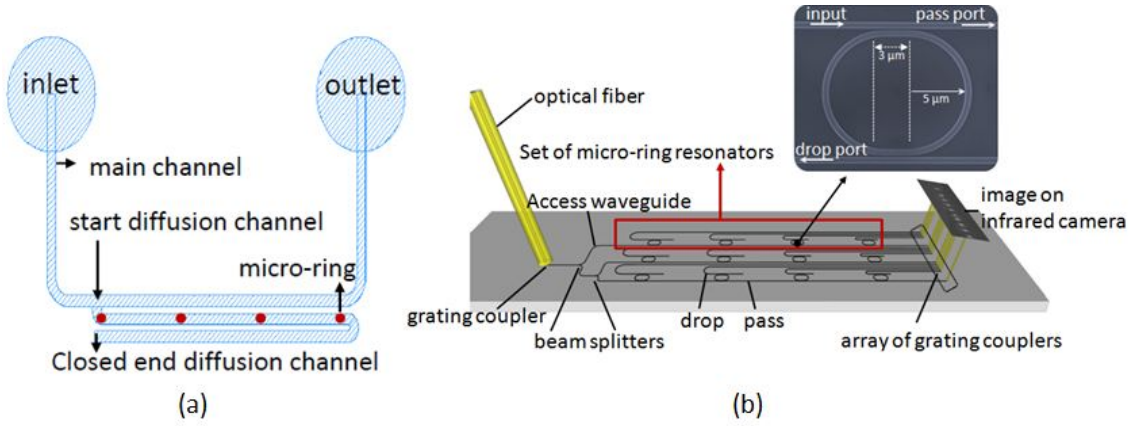

Figure 1: (a) Microfluidics design showing the main channel, from inlet to outlet, and the perpendicular diffusion channel, that encloses the ring resonator glucose sensors. (b) SOI design showing the top set of 4 micro-ring resonators that are enclosed by the micro-fluidic diffusion channel

The SOI chip is fabricated in a CMOS pilot line on a 200 mm SOI wafer, comprising a 220-nm-thick Si waveguide layer on a 2 mm buried oxide layer[2]. It contains a set of equally spaced ring resonators, with slightly increasing circumference, in add-drop configuration (see figure 1(b)). The top set of four ring resonators is enclosed by the diffusion channel. These resonators support optical modes with a wavelength λ that satisfy the resonance condition $\frac{2\pi}{\lambda}n_{eff}(\lambda)L = m \cdot 2\pi$. In which n_{eff} is the effective refractive index of the circulating mode, L the circumference of the ring and m is an integer representing the order of resonance. From the resonance condition and taking into account dispersion, a change in the refractive index of the environment, leads to a shift in the resonant wavelength according to the following equation [3]:

$$\Delta\lambda_{res} = \frac{\Delta_{env}n_{eff} \cdot \lambda_{res}}{n_g} \quad (1)$$

in which $\Delta_{env}n_{eff} = (\frac{\delta n_{eff}}{\delta n_{env}})_{\lambda=\lambda_{res}} \Delta n_{env}$ with Δn_{env} the change in refractive index in the

environment, expressed in refractive index unit (RIU) and n_g is the group index, defined as $n_g = n_{eff} - \lambda \frac{\delta n_{eff}}{\delta \lambda}$. Glucose changes the refractive index of an aqueous solution by an amount of 2e-5 RIU per mMol [4]. When a glucose solution flows through the main channel part of the glucose molecules will diffuse into the diffusion channel. The top set of four micro-rings can thus be used to detect glucose at different positions along the diffusion channel. As this channel is long but narrow, we essentially study the longitudinal diffusion.

Experimental set-up

An infrared camera set-up is used to image the output of the drop ports of the ring resonators in the diffusion channel. Laser light is coupled in and out of the chip by using grating couplers (see figure 1(b)). By tuning the laser wavelength and capturing the camera images, transmission spectra are continuously acquired. For every transmission spectrum, we fit a lorentzian curve to the resonance to determine the resonance wavelength. The wavelength shift of the resonances between consecutive measurements can then be determined. The aqueous solutions are injected through a 25-cm long polymer micro-tube in the micro-fluidics using a micro-fluidic pump. The pump speed is fixed at 10 μL/min. To switch between two solutions without generating air bubbles, we used a valve and degassed the solutions in an ultrasonic bath with a vacuum pump.

Results and discussion

We performed two distinct experiments, one with stopped flow and one with continuous flow in the main microfluidic channel. In the former case pure diffusion applies. In the latter case, we study the effect of the flow in the main channel on the speed of mass transport along the diffusion channel. The results are presented in figure 2. In the first
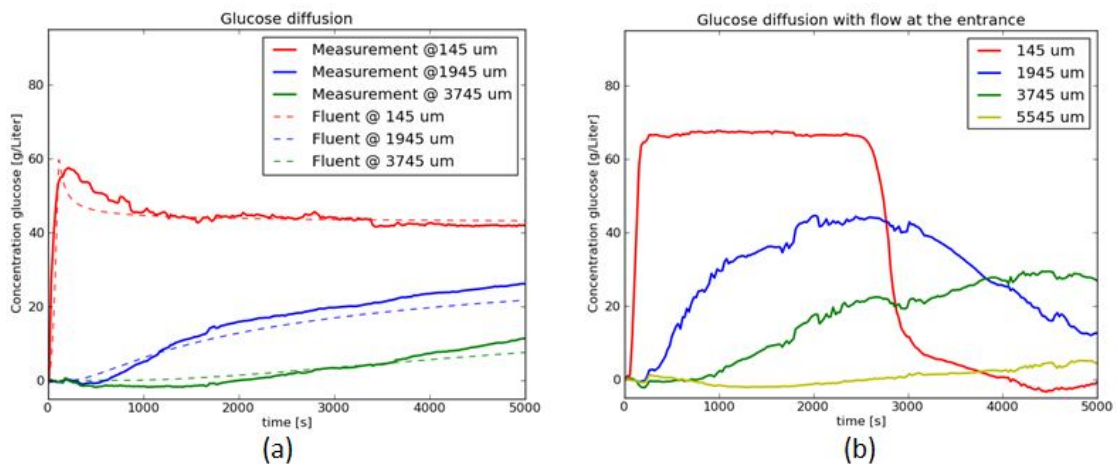

Figure 2: Glucose concentration as calculated from the wavelength shift of the microring resonances in function of time at the discrete positions of the ring resonators. (a) Experiment with stopped flow (b) Experiment with continuous flow in the main channel.

experiment we flow pure de-ionized (DI) water through the main channel and then switch the valve to a glucose solution of 90 g/L. During transport in the micro-tube a parabolic

flow profile induces a strong radial concentration gradient between the 0 g/L and 90 g/L solution. As soon as the first ring resonator shows a shift of 0.5 nm, which corresponds to a glucose level about 60 g/L, the pump is switched off. The glucose concentration at each ring is then monitored for two hours. We clearly see the fast response to glucose of the first ring, at a distance of 145 um of the main channel. The second and third ring at distances 1945 μm and 3745 μm respond slower and with a delay. The last ring at 5545 μm is used as a temperature reference for the other rings. The simulation curves are shown in the same plot. The literature value of glucose diffusion in water ($6.75 \times 10^{-10} m^2/s$ at 25°C [5]) and the exact geometry of the microfluidics and inlet tube are used. We can see a close agreement between simulations and the experimental data.

In the second experiment, we switch between the pure DI water, a glucose solution of 70 g/L and back to DI water, while keeping a steady flow through the main channel. We immediately note the faster mass transport in comparison to the first experiment. This can be explained by the driven-cavity phenomenon that occurs in viscous incompressible fluids [6, 7]. Although the diffusion channel is closed, the flow in the main channel induces convective currents. The velocity of these convective flows decreases exponentially along the diffusion channel. This situation resembles the cavity of our implant being in close contact to a flow.

Conclusion and future outlook

We designed and fabricated an opto-fluidic chip to perform glucose diffusion experiments. The results of the presented proof-of-principle experiments indicate a flexible platform to study diffusion. Also the influence of temperature on diffusion can easily be studied by using a temperature controller. A future design with more ring resonators along the diffusion channel should allow for a precise measurement of the diffusion coefficient. Furthermore, this method is not limited to glucose but paves the way for fast and accurate diffusion measurements of a variety of small molecules that dissolve in water.

Acknowledgements

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