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Chemical Engineering Journal 135S (2008) S284–S287

Chemical Engineering Journal

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Integrated IR laser system for micro-fluidic detection and analysis

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Abstract

This paper presents a novel integrated infra-red laser system ($\lambda = 1550$ nm) for micro and nano-fluidic investigation and analysis. Its principle of detection is based on attenuated total internal reflection from a diffraction grating, which is for a first time adapted and applied to operate with near infra-red laser source. The sensor is integrated in an autonomous micro-fluidic device and realized by unique fabrication technology. An analysis of aqueous solutions of sucrose is performed by the micro-fluidic chip. The response of the diffraction efficiency of the integrated detector is investigated for the strongest diffraction orders and for different light polarizations. A resolution of the sucrose concentration below 1 wt.% is achieved.

Keywords: Sensors; Methods of nanofabrication and processing; Optical constants; Chemical composition analysis

1. Introduction

Today, different kinds of lab-on-a-chip devices have been developed and applied in the chemistry, biotechnology, process control, environmental and medical sciences, etc [1]. Such systems have advantages of low-cost fabrication, high throughput, easy operation, quick processing and low consumption (∼nL) of analytes [2]. At the same time, there is an urgent necessity for development of micro-fluidic detection methods [3]. Fluorescent detection is most commonly used for monitoring of the composition. Although highly sensitive, its disadvantage is the labeling of the analytes with chromophores which sometimes changes the nature of the samples [4]. Coupling with a mass-spectrometer offers superior precision but it is too complicated, expensive and contradicts the idea of miniaturization [5]. Direct measuring techniques like ultra-violet transmission and refractometry have poor sensitivity due to the insufficient propagation path of the light [4]. A promising approach for micro-fluidic sensing offers the near infra-red (NIR) spectroscopy due to the wealth of the NIR vibration spectra [6]. It exists in two competitive varieties—IR transmission and attenuated total reflection (ATR) spectroscopy [7]. The first method is applicable for slightly absorbing fluids while the second requires stronger absorbers.

In all the aforementioned methods, the detection unit is orders of magnitude larger and more expensive than the micro-chip. For micro-fluidic sensing, it is preferable the detection part to be integrated in the chip. Furthermore, the chip should be sensitive to all components of the analyte and in the same time not to interact with them or change them. The goal of the presented work is to develop a novel integrated IR laser system for micro and nano-fluidic analysis. Its principle of operation is based on the diffraction under total internal reflection (TIR) condition, thus can be considered as a modified ATR. For the first time such a diffraction grating (DG) configuration has been described in [8]. Previous investigations with a visible monochromatic light source prove that small changes of the optical constants of the investigated liquid cause linear changes in the diffracted energy [9–11]. Applications of a DG for visible spectroscopic studies and investigations of liquid media, as well as a numerical simulation for its diffraction can be found in [12,13]. Very recently, the TIR-DG has been integrated as a detection unit in a micro-fluidic chip [14,15], but was still used in conjunction with a visible (red) diode laser. In the present work, the TIR–DG sensor has been for a first time to our knowledge adapted for operation with NIR laser light. The detector is integrated on an autonomous

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doi:10.1016/j.cej.2007.07.041

micro-fluidic chip. The sensor is applied for concentration analysis of aqueous solutions of sucrose, which absorb NIR light. The sensitivity of the senor is determined and approaches for its improvement are discussed.

2. Experimental

The fabrication of the sensor is illustrated in Fig. 1. The device is created by sealing of two wafers, called prism and channel wafers. In both cases (1a and 2a), double-side polished, oxidized Si ⟨1 0 0⟩ wafers are used. First, the SiO_2 of the bottom of the prism wafer is removed. With a lithographic step for the grid (1b), Al deposition and consequently, a lift-off of the metal (1c) the DG is realized. Then the oxide from the front side is patterned by lithography and a SiO_2 etch step, defining the topside of the prism (1d). The bulk Si micro-prism is created by anisotropic Si etch in KOH (1c) at 60 °C, while the grating side of the wafer is protected with a chuck (1e). The KOH etch is stopped when the etched Si areas begins to transmit dark-red light, resulting in a 20 μm residual silicon membrane. The oxide on both sides of the channel wafer is patterned by a double-sided lithography and SiO_2 etch, defining the etch mask for the following bulk micromachining (2b). Then the wafer is double-sided etched in KOH until the two etch fronts get together, forming simultaneously the micro-channel and the in-let and out-let openings (2c). Finally, the micro-fluidic chip (1 + 2) is created by bonding of the two wafers.

Fig. 2a shows a 3D view of the micro-fluidic chip during measurements while Fig. 2b represents the optical setup. The basic light source is a NIR diode laser with λ = 1550 nm (1). Polarization parallel (p) or perpendicular (s) to the plane of incidence is adjusted by a polarizer (3). The NIR beam is coupled with the beam of a red diode laser (2) by a beam-splitter (4), which allows easily optical adjustment. The incident beam is directed to the prism facet. It fulfills the TIR condition for the interface between the micro-prism (5) and the fluid in the micro-channel (7), where the metal diffraction grating (6) is situated. The fluidic sensing is realized with the help of the evanescent electromagnetic field, which penetrates in the investigating medium from the spacing between the lines of the grid. The conversion of the harmonic waves into the evanescent TIR field at the two media interface, caused by the dielectric discontinuity of the media, is influenced by the optical constants of the micro-fluid. At the same time the reflection from the lines of the grating creates a constant reference signal. The diffraction pattern (8) is crated as a result of the interference of the light, reflected from the lines and from the spacings. The changes in the optical constants of the fluid are detected by measuring the diffraction efficiency (DE) of the 0th (η_0) and the 1st (η_1) order. This is realized by fixed photodetectors, since the angles of diffraction are constant [10,11].

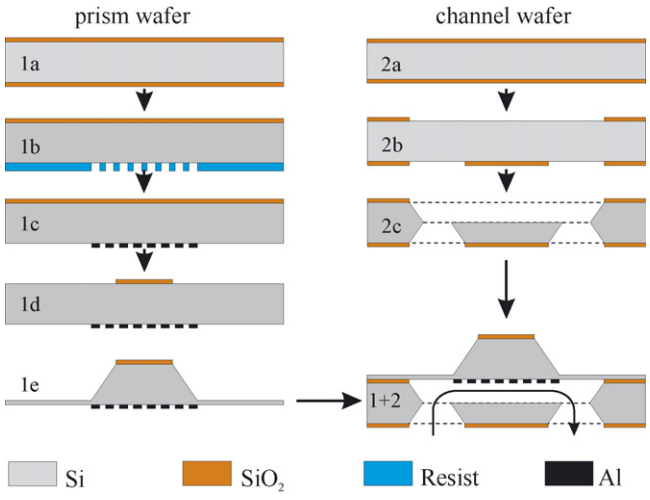

Fig. 1. Fabrication of the integrated micro-fluidic sensor.

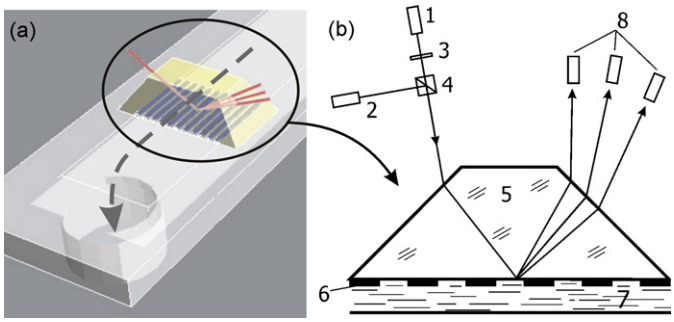

Fig. 2. (a) 3D view of the micro-fluidic chip during measurements; (b) optical setup: 1, NIR laser; 2, red laser; 3, polarizer; 4, beamsplitter; 5, Si prism; 6, DG; 7, μ-channel; 8, detectors.

3. Results and discussion

A picture of the fabricated integrated micro-fluidic chips is shown in Fig. 3a. Fig. 3b presents the sensor chip, placed in its holder, which ensures the micro-fluidic supply. The application of silicon IR optical elements benefits by the simplicity of a monolithic Si fabrication and a compatibility with the developed SMOS technologies, which results in cheap and high throughput. Although Si is transparent for λ from 1.1 to 15 μm, its application as an IR optical material leads to high reflection losses (∼50% from the both facets of the Si prism) due to the high Si refractive index (RI) $n_{Si} \sim 3.5$. On the other hand the TIR condition is satisfied practically for any external angle of incidence.

Critical issues for proper sensing are the flatness of the TIR interface, the quality of the prism walls and the grating's lines roughness. The first is defined by the roughness of the Si wafer (Fig. 1, step 1c), which is typically below 1 nm. The prism's facets are formed by wet KOH anisotropic etching (step 1e), which is a known method for bulk micro-structuring, resulting in a smooth surface [14]. Thus, the quality of the prism facets is better than λ/4. Only prisms with refracting angle of 54.74° can be prepared by KOH anisotropic etch of ⟨100⟩ silicon. The grating's roughness depends on the lithography limits. A line quality of 0.25 μm related to a period of 10 μm clearly defines the diffraction pattern. It is worthy to point out, that the fabrication sequence is improved in this work and allows realization of the micro-fluidic body from a single wafer and forming of the channel and the nozzles simultaneously by a single etch step.

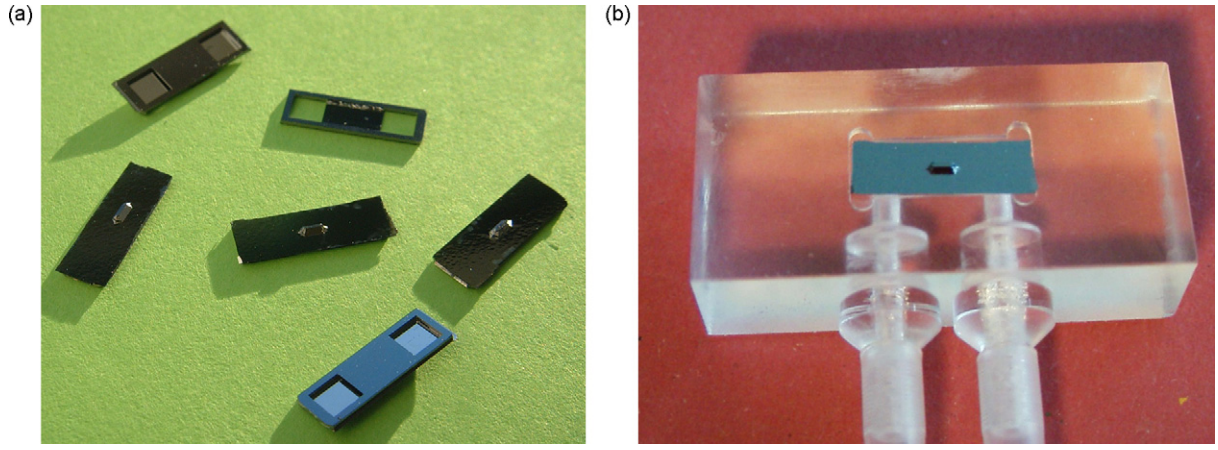

Fig. 3. (a) Picture of the fabricated integrated IR sensors, (b) a sensor chip placed in a micro-fluidic holder.

The sensing possibilities of the integrated micro-fluidic detector are investigated with the help of aqueous solutions of sucrose with a concentration up to 20 wt.%. Such an analyte is chosen due to several reasons. First it possesses a smooth absorption spectrum and a high value of the molar absorptivity in the NIR region for wavelengths between 1.4 and 1.8 μm. Furthermore, the sucrose solutions are easy to prepare and handle and are not harmful. The NIR absorption of sucrose, fructose and glucose is well studied: NIR spectroscopic methods are applied for determination of glucose content in the human blood [16] and fructose content in fruits [17].

The sensor response towards changes in the sucrose concentration c is plotted in Fig. 4. The measurements are taken in the 0th and 1st order and for s (Fig. 4a) and p polarization (Fig. 4b). The experimental points are fitted with linear functions, represented by the dashed lines in Fig. 4. In all cases, the linear fit agrees with the data within the 1% relative measurement error (shown as error-bar in the figures), as could be expected according to the Beer's law.

Fig. 4 shows, that the DE η of all orders and for any direction of the polarization decreases. The previous analysis [14,15] shows, that the result is connected to the increased absorption losses, which attenuates the TIR from the transparent parts of the DG. On the other hand the DE distribution is also influenced by the RI variation due to the changes in the concentration. Finally the diffraction orders have a different sensitivity to the fluidic optical constants depending on the parameters of the grating and the light [15]. Thus, the measured DE response should be assigned to the combined effect of the change of the real and imaginary part of the RI and the particular sensor configuration. But the phase change of the TIR light, caused by the fluidic RI variation, should be comparatively small due to the large angular deviation from the critical angle. Therefore, the absorption changes should be considered dominant for the response of the integrated detector.

The absorption of the water in the whole NIR region cannot be neglected. This fact has to be taken into account for any experiments with water-derivative biochemical and microbiological samples. In particular, the DE of the sensor at $c = 0$ correspond to the native H_2O absorption at $\lambda = 1550$ nm. It is determined by the proximity of the first overtone band of the OH stretching mode (1450 nm = 1/2*6900 cm^{-1}), which is assigned to the hydrogen bonded OH peak [6,18]. Thus, the observed DE change is related to the difference between the molar absorptivity of the water

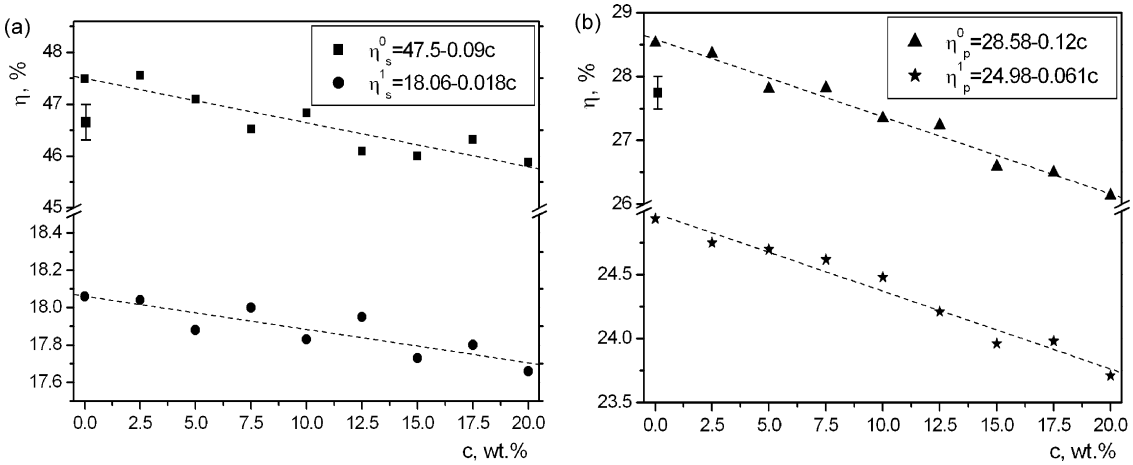

Fig. 4. Diffraction efficiency dependence on the concentration of aqueous sucrose solutions: (a) s polarization, (b) p polarization of the light. The dashed lines are linear fits.

Table 1
DE sensitivity and resolution for sucrose concentration

	s polarization		p polarization	
	0th order	1st order	0th order	1st order
$d\eta/dc$	−0.09	−0.018	0.12	0.061
Δc, wt.%	1.1	5.5	0.8	1.6

and sucrose. Thereby, the led experiments should be considered as differential measurements and thus are not disturbed by the absorption at zero concentration.

The DE sensitivity $d\eta/dc$ for the different combinations between light polarization and examined diffraction order are summarized in Table 1. Measurements with p polarizations seem to be advantageous due to the larger DE gradient. For both polarizations, the DE response is higher for the 0th order, but studying the 1st order is beneficial due to the highest signal-to-noise ratio, since it is free from the geometrical reflection and the parasitic scattered light propagating in proximity to the 0th order. The results of this investigation can be applied for concentration analysis. The resolution of sucrose concentration Δc is given by $\Delta c = |d\eta/dc|^{-1}\Delta\eta$. The calculated values are given also in Table 1. The most sensitive measurements are made in the 0th order for p polarization, when a concentration resolution below 1 wt.% is achieved. The relative sensitivity can be improved by using denser solutions, fluids with higher refractive or absorption indices, illuminating the prism/fluidic border at higher angle of incidence. It is also beneficial to measure the signals from the photodetectors in a differential regime.

4. Conclusions

A novel integrated IR laser system for micro and nano-fluidic investigation has been developed in this work. The sensing is realized by diffraction under TIR condition. Main technological advantages of the presented micro-fluidic detector are the simplified monolithic fabrication technique and the fixed positions of the laser and the photodetectors (i.e. there are no moving parts) and the operation with a monochromatic NIR source (i.e. no spectral analyzer is required). Additional benefits are the sensitivity to both the real and imaginary part of the RI and the possibilities to measure strongly absorbing and highly concentrated solutions. The micro-fluidic sensor is applied for investigation of aqueous solutions of sucrose. A resolution of the sucrose concentration better than 1 wt.% is achieved. Envisioned applications of the integrated micro-sensor are chemical, medical and biological diagnostic of liquid substances and dispersions of drugs, serums, proteins, peptides, DNA, RNA, etc.

Acknowledgments

The work is supported by the AvH Foundation and grants VEGA No. 2/4008/04 and APVT No.APVT-20-017304.

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