Photonic Integrated Circuits for Refractive Index-Based Detection in Liquid Chromatography

J.H. Mendoza-Castro[1], D. Tomasetig[1], S. Schobesberger[2], A.S. Vorobev[3,4], G. Ricchiuti[1,3,4], A. Dabrowska[1], S. Iadanza[5,6], M. Grande[7], G. Magno[7], L. O'Faolain[3,4] and B. Lendl[1]

1. Institute of Chemical Technologies and Analytics, TU Wien, Getreidemarkt 9/164, Vienna, 1060, Austria
2. Institute of Applied Synthetic Chemistry, TU Wien, Getreidemarkt 9/164, Vienna, 1060, Austria
3. Centre for Advanced Photonics and Process Analysis, Munster Technological University, T12 T66T Bishopstown, Cork, Ireland
4. Tyndall National Institute, T12 PX46 Cork, Ireland
5. Laboratory of Nano and Quantum Technologies, Paul Scherrer Institut, 5232, Villigen, Switzerland
6. Laboratory of Integrated Nanoscale Photonics and Optoelectronics, EPFL, 1015 Lausanne, SwitzerlandSchweiz
7. Department of Electrical and Information Engineering, Politecnico di Bari, Via E. Orabona, 4, 70126 Bari, Italy
jesus.mendoza-castro@tuwien.ac.at

***Abstract*—We demonstrate the on-chip integration of silicon nitride refractive index transducers with microfluidics for refractive index-based detection in liquid chromatography, highlighting the system's potential for creating compact, highly sensitive, and selective sensors capable of analyzing a wide range of complex liquid samples and analytes.**

***Keywords*—HPLC, spectroscopy, silicon nitride, refractive index sensing, micro ring resonator, optical sensing.**

I. INTRODUCTION

Refractive index (RI) sensors are fundamental tools in analytical chemistry, particularly in high-performance liquid chromatography (HPLC). They enable non-destructive detection of changes in solution composition, making them valuable in fields ranging from biochemical analysis to environmental monitoring. RI sensors are especially useful when samples lack strong chromophores (UV-VIS) and are nonfluorescent. However, traditional RI detectors are bulky, with limited dynamic range, and highly sensitive to thermal fluctuations which restrict their use in high-sensitivity and gradient elution applications. This drives the need for more compact, sensitive, and thermally stable RI detection technologies. Silicon photonics, with its potential for miniaturization and enhanced sensitivity, has emerged as a promising platform for integrated RI sensors [1]. Micro Ring Resonators (MRRs) are attractive for their high sensitivity to RI variations, on-chip integration and scalable manufacturing processes.

In this work we experimentally investigate a Si_3N_4 refractive index transducer based on MRRs [2], designed through 3D-FDTD simulations and operating in the C Optical communication band. This transducer functions as a non-destructive and universal detector for liquid chromatography. The Si_3N_4 RI transducer is interfaced with custom-developed microfluidics, leading to reduced band broadening, due to miniaturized channel dimensions, enabling much smaller sample volumes and faster analysis. To demonstrate the system's capabilities, a proof-of-concept isocratic elusion separation is performed. This approach allows the development of portable on-site testing devices applicable in various fields even beyond chromatography like photothermal spectroscopy [3], [4].

II. DESIGN AND FABRICATION

Micro ring resonators were designed to operate at 1550 nm based on our previous work [2]. These microcavities were fabricated on a thermally oxidized silicon wafer, featuring a 2.2 µm thick buried oxide (BOx) layer, with a 300 nm thick Si_3N_4 layer deposited via plasma-enhanced chemical vapor deposition (PECVD). The device layouts were patterned using electron beam lithography (EBL) at 100 kV, and the patterns were transferred to the Si_3N_4 layer through inductively coupled plasma (ICP) etching. Microfluidic channels were structured in a pressure-sensitive adhesive (PSA), and a bonding mechanism was developed to integrate the microfluidics on top of the released Si_3N_4 chip, along with a thicker layer of Polydimethylsiloxane (PDMS). Additionally, a liquid handling system was implemented to ensure precise fluid manipulation for the experiments.

III. EXPERIMENT

Figure 1(a) provides a schematic of the experimental setup, accompanied by real-view insets shown in Figure 1(b), (c). The probe beam, a NIR laser, was coupled into the waveguide via a fibre system and spot-size converting lenses. The spectral response of the RI transducer was collected by a photodetector at the output. Figure 1(b) offers a detailed view of the assembly, where the light path and fluid flow are perpendicular. A thermally stabilized holder supports the setup from below, while an apochromatic microscope objective enables inspection of the microfluidic channel and scattered light from above when the device is illuminated. The RI transducer, depicted in Figure 1(c), is a MRR [2] used to interrogate the refractive index variations occurring in the top surface.

Refractive index sensing was demonstrated using aqueous glucose solutions with concentrations from 10 to 50 mg/mL, in 10 mg/mL increments. The holder was temperature stabilized at 24 ± 0.002°C, matching the lab conditions (~24°C, 56% humidity). Measurements were taken at a constant flow rate of 70 µL/min. The spectral response of the MRR, shown in Figure 1(c), highlights resonances for a 10 mg/mL glucose

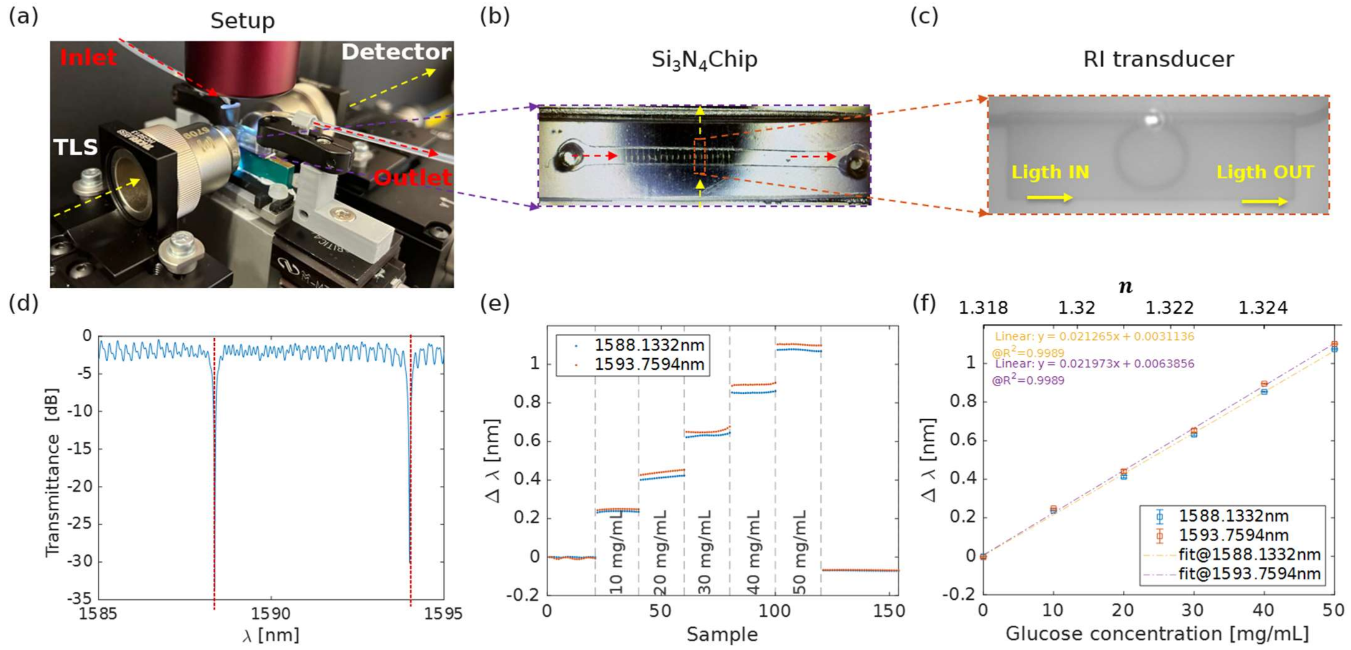

Fig. 1. (a) Detailed view of the experimental setup, showing the interface between the liquid handling system and the optical readout components, including the Tunable Laser Source (TLS) and the detector. The red and yellow dashed arrows indicate the flow direction of the liquid and light, respectively. (b) Top view of the fabricated microfluidic channel bonded to the Si_3N_4 chip. (c) Close-up view of the refractive index transducer (MRR), where light scattering within the device is observed as a steady liquid flow moves from top to bottom, while light is coupled from left to right. (d) Transmission spectrum of a sample MRR device with a 10 mg/mL glucose solution flowing over the chip. The red dashed lines mark the resonant wavelengths of the MRR. (e) Resonance wavelength shifts, with respect to the reference (H_2O), as glucose concentration increases from 10 to 50 mg/mL, followed by a water flush. (f) Calibration curves corresponding to the measurements in (e).

solution, with vertical red lines marking the resonance minima used to track wavelength shifts as concentrations varied. These shifts, shown in Figure 1(e), were translated into a calibration curve (Figure 1(f)) based on refractive index values from [5]. Sensitivities of ~138 nm/RIU and ~142 nm/RIU confirm successful integration of the microfluidic system with the refractive index transducer.

The developed refractive index transduction mechanism was integrated with an HPLC system. Isocratic elution separations were performed using well-characterized sugar mixtures, such as glucose and fructose, to demonstrate the utility of the integrated transducer as detector in liquid chromatography. The successful separation of a four-sugar mixture was achieved, illustrating the ability of photonic integrated circuits (PICs) to perform isocratic elution separations under ambient conditions. This approach can overcome two key limitations of conventional RI-based detectors—limited dynamic range and prolonged thermal stabilization time—while maintaining comparable bulk refractive index sensitivity. Further details of the separation experiments will be discussed.

IV. Conclusion

In this work, we developed and integrated silicon nitride refractive index transducers with microfluidics for use as a detector in high performance liquid chromatography (HPLC). The characterization of the RI transducers, based on MRRs [2], in the proposed setup benefits from defined and highly reproducible sensor analyte interaction. The developed RI sensor enables detection in small volumes as demonstrated by the successful quantification of sugars separated by HPLC. PIC-assisted HPLC allow for a broad dynamic range requiring minute sample amounts. The developed platform can incorporate also other transducers [6], offering an avenue for highly sensitive detection in photothermal spectroscopy [3], [4].

Acknowledgment

The authors gratefully acknowledge the European Union's Horizon 2020 research and innovation programme under the Marie Skłodowska-Curie grant agreement No 860808 (OPTAPHI) and the CINECA award under the ISCRA initiative, for the availability of high-performance computing resources and support (projects ASTREA and METAFORE).

References

[1] J. H. Wade and R. C. Bailey, "Refractive Index-Based Detection of Gradient Elution Liquid Chromatography using Chip-Integrated Microring Resonator Arrays," *Anal. Chem.*, vol. 86, no. 1, pp. 913–919, Jan. 2014, doi: 10.1021/ac4035828.

[2] J. H. Mendoza-Castro, A. S. Vorobev, S. Iadanza, B. Lendl, L. O'Faolain, and M. Grande, "Enhanced Fano resonances in a silicon nitride photonic crystal nanobeam-assisted micro ring resonator for dual telecom band operation," *Opt. Express, OE*, vol. 32, no. 8, pp. 13197–13207, Apr. 2024, doi: 10.1364/OE.504912.

[3] G. Ricchiuti *et al.*, "Photothermal spectroscopy on-chip sensor for the measurement of a PMMA film using a silicon nitride micro-ring resonator and an external cavity quantum cascade laser," *Nanophotonics*, Mar. 2024, doi: 10.1515/nanoph-2024-0033.

[4] M. V. Kotlyar, J. J. Mapranathukaran, G. Biagi, A. Walsh, B. Lendl, and L. O'Faolain, "Micro-Ring Resonator Assisted Photothermal Spectroscopy of Water Vapor," *Sensors*, vol. 24, no. 11, Art. no. 11, Jan. 2024, doi: 10.3390/s24113679.

[5] L. Castelló-Pedrero, M. I. Gómez-Gómez, J. García-Rupérez, A. Griol, and A. Martínez, "Performance improvement of a silicon nitride ring resonator biosensor operated in the TM mode at 1310 nm," *Biomed. Opt. Express, BOE*, vol. 12, no. 11, pp. 7244–7260, Nov. 2021, doi: 10.1364/BOE.437823.

[6] S. Iadanza *et al.*, "High-Q asymmetrically cladded silicon nitride 1D photonic crystals cavities and hybrid external cavity lasers for sensing in air and liquids," *Nanophotonics*, vol. 11, no. 18, pp. 4183–4196, Sep. 2022, doi: 10.1515/nanoph-2022-0245.