

# Measurement of paracetamol concentration using a fiber laser system

Liliana Soares

*INESC TEC - Institute for Systems and Computer Engineering, Technology and Science*

*Faculty of Engineering, University of Porto*  
Porto, Portugal  
liliana.p.soares@inesctec.pt

Rosa Ana Perez-Herrera

*Department of Electrical, Electronic and Communication Engineering, Public Univ. of Navarra*

*ISC - Institute of Smart Cities, Public Univ. of Navarra*  
Pamplona, Spain  
rosa.perez@unavarra.es

Susana Novais

*INESC TEC - Institute for Systems and Computer Engineering, Technology and Science*

*Porto, Portugal*  
susana.novais@inesctec.pt

António Ferreira

*LEPABE—Laboratory for Process Engineering, Environment, Biotechnology and Energy, University of Porto*  
*ALiCE -Associate Laboratory in Chemical Engineering, University of Porto*

*Porto, Portugal*  
antonio@fe.up.pt

Orlando Frazão

*INESC TEC - Institute for Systems and Computer Engineering, Technology and Science*

*Porto, Portugal*  
orlando.frazao@inesctec.pt

Susana Silva

*INESC TEC - Institute for Systems and Computer Engineering, Technology and Science*

*Porto, Portugal*  
susana.o.silva@inesctec.pt

**Abstract**—A linear fiber laser system for measurements of paracetamol concentration is experimentally demonstrated. The cavity is based on a fiber loop mirror and an FBG centered at 1567.8 nm. The sensing head corresponds to a refractometric sensor, whose principle of operation is based on Fresnel reflection in the fiber tip (FBG side). The system works at detected variations of paracetamol concentrations with a sensitivity of  $[(8.74 \pm 0.34) \times 10^{-5}] \mu\text{W}/(\text{g}/\text{kg})$  and a resolution of 2.77 g/kg. The results prove that the fiber laser system could be an asset for processing industries, specifically for non-invasive and real-time measurements of concentration.

**Keywords**—*fiber laser, paracetamol, concentration, processing industries*

## I. INTRODUCTION

In the past years, refractive index measurement has performed a significant role in processing industries, such as pharmaceutical, chemical, biological, medical, foody industry and environmental [1]. The growth of research and development in this field is driven by the need for quality control, which is often required by the end consumer [2].

Optical fiber sensors are a promising tool for refractive index sensing, due to their desirable features, such as reduced dimensions, compatibility, and high degrees of integration, which allow to provide real-time measurements in a non-invasive and non-destructive way [3], [4]. Different configurations and mechanisms of fiber optic refractive index sensors have been proposed and developed. They are sensitive to the refractive index variations in the surroundings of the fiber surface and these variations modify the light propagation, which cause changes in the transmission or reflection spectra [5].

For more than a century, the measurement of concentration has been particularly important in processing industries for optimize the production [5]. In this way, this type of refractometric sensors have been specially used to determine the material concentration.

The sensibility of the technology used in this process can improve all type of refining, manufacturing, and quality control operations. For this, real-time measurements are the most appealing, because they avoid sample preparation and time delays [4].

This work proposes and demonstrates a fast and simple technique to measure the concentration of liquid solutions. Paracetamol was chosen as a case study because it is a well-known analgesic and antipyretic in the pharmaceutical field. The technique presented is based on a refractometric sensor, implemented through a linear cavity-based fiber laser system. The fiber laser system performs real-time measurements of concentration in a non-invasive and non-destructive way, presenting a potential to optimize the production in processing industries, such as the pharmaceutical, by maximizing the use of reagents, avoiding the production of waste and, consequently, ensuring the cost reduction.

The main advantage of this proposed system is the possibility of multiplexing several sensor fiber tips placed in different measurement sites, without changing the interrogation system. In this way, it can be used for different applications requirements, in a simple and low-cost way, compared to other process analytical technologies.

## II. EXPERIMENTAL SETUP

In this work a fiber laser system is proposed to performed measurements of paracetamol concentration in liquid solutions. The configuration used is presented in Fig. 1.

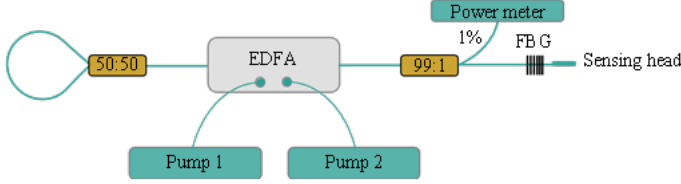


Fig. 1. Experimental setup of the fiber laser system.

The laser gain of the system was provided by a commercial bidirectional Erbium-Doped Fiber Amplifier (EDFA) from MWTechnologies. As it is possible to see in Fig. 1, the bidirectional EDFA used consists of two 3-port optical circulators and two conventional EDFAs (i.e., an erbium-doped fiber and a co-directional pump). Each pump of the conventional EDFAs could be independently controlled. To obtain a linear cavity, two distinct mirrors are used: a fiber loop mirror and a Fiber Bragg Grating (FBG). The use of two different mirrors allows obtaining an increase in the Amplified Spontaneous Emission (ASE) generated by the fiber tip and simultaneously the emission stimulated by the FBG mirror. The FBG used corresponds to a commercial grating, centered at 1567 nm, with a reflectivity of 97.59% and a bandwidth of 0.243 nm at  $-3$  dB.

To acquire the laser optical power, a 99:1 optical coupler was used. In the measurements performed, 1% of the system signal was extracted to a power meter (model Agilent 8163B).

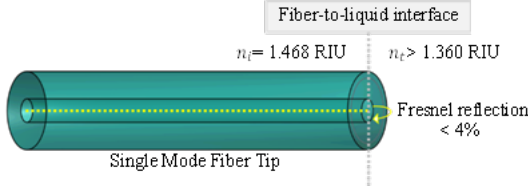


Fig. 2. Scheme of the sensing head operating mechanism.

In this configuration, the sensing head corresponded to the fiber tip where the FBG was located – Fig. 2. It was cleaved at 20 mm after the FBG, because its operating mechanism relies on the Fresnel reflection. In this way, it is operating related to the measurand-induced intensity variation of the Fresnel reflection at the fiber-to-liquid interface monitored. When the light reaches the surroundings (see Fig. 2), it is partially reflected and, according to the liquid refractive index variations, the intensity of the reflected optical signal linearly changes. Through the Fresnel equation (1) for a reflection at a normal incidence, it is possible to calculate the Reflectance,  $R$ , which corresponds to the ratio between the reflected light in the fiber-to-liquid interface and the incident light [6]:

$$R = (n_t - n_i / n_t + n_i)^2 \quad (1)$$

Since the refractive index of the fiber optic core ( $n_i = 1.468$  RIU) has a higher value than the refractive index of paracetamol liquid solutions ( $n_t > 1.360$  RIU), and according to (1), less than

4% of the light guided by the fiber is reflected at the fiber-to-liquid interface monitored.

## III. RESULTS

### A. Output spectrum

The fiber laser system was characterized using an Optical Spectrum Analyzer (OSA, YOKOGAWA, model AQ6370D). The output spectrum of the fiber laser system is shown in Fig. 3. The maximum output power level was measured with an Optical Signal to Noise Ratio (OSNR) of 54 dB and it corresponds to the FBG filter: centered at 1567.8 nm and with an output power level of  $-12$  dBm.

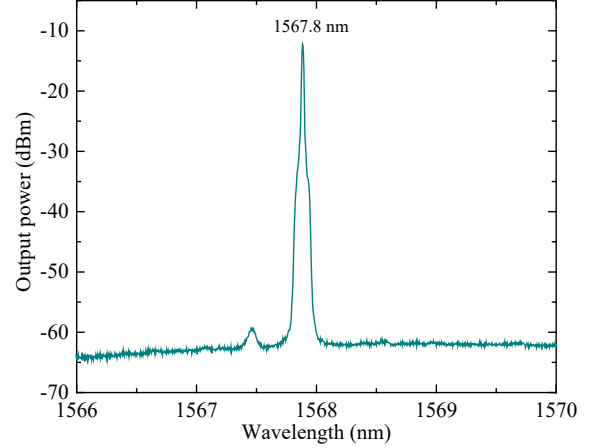


Fig. 3. Fiber laser system output spectra.

### B. Sensitivity of fiber laser system

Eight standard liquid solutions of paracetamol with a concentration range of 52.61 to 219.25 g/kg were measured using the laser configuration proposed. The paracetamol was dissolved in a mixture of 40% (v/v) ethanol/water. For the measurements, the sensing head was vertically immersed in each paracetamol sample and the sensor response was obtained using the power meter. As it is possible to see in Fig. 4, it was obtained a linear sensitivity of  $[(8.74 \pm 0.34) \times 10^{-5}] \mu\text{W}/(\text{g}/\text{kg})$  to the variation of paracetamol concentration, with ranges of 52.61 to 219.25 g/kg.

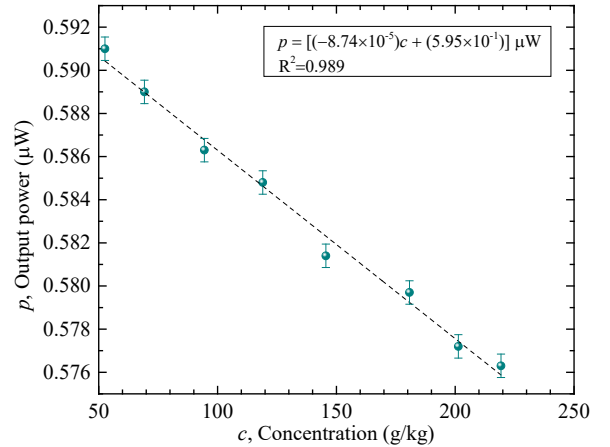


Fig. 4. Output power level as a function of paracetamol concentration.

### C. Resolution of fiber laser system

The resolution of the system was determined using two samples of paracetamol with consecutive values of concentration, 52.61 g/kg and 69.21g/kg, respectively. The sensing head was successively immersed in the referred samples, and the sensor response was recorded using an optical power meter – Fig. 5.

According to the sensor response, the resolution of the system, i.e., the minimum value of concentration ( $\delta_c$ ) that the system can discriminate, was calculated through the (2) [7]:

$$\delta_c = 2 \frac{\sigma_p \Delta c}{\Delta P} \quad (2)$$

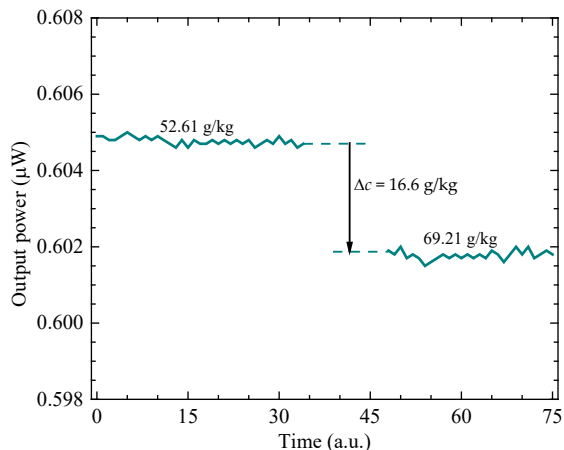


Fig. 5. Evaluation of system resolution using two consecutive measurements.

where  $\sigma_p$  is the maximum standard deviation of the output power ( $2.5 \times 10^{-4} \mu\text{W}$ ) for both values of concentration (52.61 g/kg and 69.21 g/kg),  $\Delta c$  is the variation of concentration (16.6 g/kg), and  $\Delta P$  is the mean displacement of output response between the two steps ( $3.0 \times 10^{-3} \mu\text{W}$ ). A value of 2.77 g/kg was obtained for the system resolution. It is important to refer that this value was also influenced by the spectral resolution of the equipment used for data acquisition (0.01 pW).

### IV. CONCLUSION

In this work, a fiber laser sensor system has been proposed and experimentally demonstrated to performed concentration measurements in paracetamol liquid solutions. The sensing head of the system corresponded to a refractometric sensor capable of measuring the laser optical power as a function of the concentration.

The experimental results indicated that the optical power of the proposed system varied linearly with the concentration of paracetamol within the range of 52.61 to 219.25 g/kg, yielding a sensitivity of  $[(8.74 \pm 0.34) \times 10^{-5}] \mu\text{W}/(\text{g}/\text{kg})$  and a resolution of 2.77 g/kg.

The proposed fiber laser sensor system is a simple configuration, it can be easily implemented to performed in-line liquid measurements of concentration for the purpose of process control in processing industries.

### ACKNOWLEDGMENT

This research was funded by: This research was funded by: This work was financially supported by the Wellcome Trust, UK, through the Innovator Award “Light-activated cap for catheter sterilization” (WT223940/Z/21/Z); National Funds through FCT/MCTES (PIDDAC), within projects LA/P/0045/2020 (ALiCE), UIDB/00511/2020 and UIDP/00511/2020 (LEPABE); Program “José Castillejo para estancias de movilidad en el extranjero de jóvenes doctores”, funded by the Ministerio de Univesidades of Spain (reference CAS21/00351); project PID2019-107270RB-C22, funded by MCIN/AEI/10.13039/501100011033 and FEDER “A way to make Europe”; projects PDC2021-121172-C21 and TED2021-130378B-C22 funded by MCIN/ AEI/10.13039/501100011033 and European Union “Next generation EU”/PTR. Liliana Soares acknowledges the support of FCT, Portugal, through the Grant 2020.05297.BD.

### REFERENCES

- [1] R. Gosselin, P. Durão, N. Abatzoglou and J.-M. Guay “Monitoring the concentration of flowing pharmaceutical powders in a tableting feed frame,”*Pharm. Dev. Technol.*, vol. 22, n° 6, pp. 699-705, 2017.
- [2] J. Harting and P. Kleinebudde “Optimisation of an in-line Raman spectroscopic method for continuous API quantification during twin-screw wet granulation and its application for process characterization,”*Eur. J. Pharm. Biopharm.*, vol. 137, n° 2, pp. 77-85, 2019.
- [3] Y. Gao, T. Zhang, Y. Ma, F. Xue, Z. Gao, B. Hou and J. Gong “Application of PAT-Based Feedback Control Approaches in Pharmaceutical Crystallization,”*Crystals*, vol. 11, n° 3, 221, 2021.
- [4] E.J. Kim, J.H. Kim, M.-S., Kim, S.H. Jeong and D.H. Choi “Process Analytical Technology Tools for Monitoring Pharmaceutical Unit Operations: A Control Strategy for Continuous Process Verification,”*Pharmaceutics*, vol. 13, n° 6, 919, 2021.
- [5] J. Wiss, “Process Analytical Technology: tools and applications in pharmaceutical manufacturing,”*Chim. Oggi Chem. Today*, vol. 33, n° 2, pp. 30-33, 2015.
- [6] E. Hecht, *Optics*, 5th ed. Pearson: London, UK, 2015.
- [7] L. Soares, S. Novais, A. Ferreira, O. Frazão and S. Silva, “Detection of the Crystallization Process of Paracetamol with a Multi-Mode Optical Fiber in a Reflective Configuration,”*Sensors*, vol. 20, n° 1, 87, 2019.