Waveguide Raman Sensing for Chemical Detection in Industrial Processes

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Abstract: Waveguide-enhanced Raman spectroscopy (WERS) is a promising method for detecting chemical and biological compounds with high sensitivity and selectivity on a chip-scale platform, but has so far been limited to demonstrations in research laboratories. We present the implementation of a fibre-coupled WERS sensing system in an industrial bioproduction process.

1. Introduction

Waveguide-enhanced Raman spectroscopy (WERS) combines the principles of Raman spectroscopy with integrated photonics technology to perform Raman spectroscopy on a miniaturized and integrated scale, yielding performance, cost, and size benefits compared to traditional Raman spectroscopy based on a free-space interaction [1]. These benefits are highly relevant to industrial applications, some of which already commonly rely on Raman spectroscopy for e.g. raw material authentication or real-time chemical monitoring [2]. However, the demonstrations of WERS chemical sensing have so far consisted in bringing the sample to the sensor rather than implementing the sensor in the actual environment to be measured. This is notably due to the degradation in performance associated with fibre-coupling of WERS chips because of the fibre-induced background. Here we present a fibre-coupled WERS sensing system with background reduction and correction allowing for its use in industrial applications, and demonstrate its implementation for the monitoring of an industrial fermentation process.

2. Practical fibre-coupled WERS sensors

The challenge of fibre-coupled WERS lies in the background signals generated in the fibre and core of the waveguide, that reduce the signal-to-noise ratio (SNR). Backscattered collection allows to tackle this issue by collecting the Raman signal emitted in the opposite direction to the excitation light: the excitation light and the input fibre and waveguide Raman signals, which propagate forward, are effectively filtered out (notwithstanding the fraction of these signals that is backscattered due to e.g. sidewall roughness). Backscattered collection is easily implemented on-chip with a 50/50 coupler, e.g. a multi-mode interferometer (MMI). An improvement to this strategy consists in using, or adding, a wavelength-selective coupler to remove the excitation light more efficiently from the collected signal. Beyond background filtering, fibre-coupled WERS also relies on the implementation of key on-chip components such as low-loss waveguides and efficient optical fibre-to-chip couplers. With state-of-the-art values for each of these components, an improvement over traditional Raman probes of several orders of magnitude can be achieved [3]. The sensors used in this study use an MMI as 50/50 coupler for backscattering collection, inverse tapers for fibre-to-chip coupling, and 300nm-thick silicon nitride waveguides exhibiting losses around 1 dB/cm.

For practical implementation outside of optical research laboratories, additional building blocks are required: the photonic integrated circuit (PIC) sensor ought to be integrated into a mechanical package that allows for connection to the measurement environment, and the acquired spectra ought to be treated by a signal processing software that corrects the specific features of WERS spectra, mostly the remaining background. An example of a flow cell is shown on Fig. 1.b). To remove the background, a wide variety of fitting algorithms have been developed to isolate the peaks of the species under analysis. However, these algorithms require hypotheses on the nature of the analyte(s) (notably, where the peaks are expected to appear) to prevent from overfitting. Another possibility is to measure without the analyte first, in order to obtain a reference spectrum that can then be subtracted from the analyte spectrum – yet such a reference measurement is not always possible. To avoid this issue, we use a background subtraction algorithm that only requires knowing the refractive index of the medium to be analysed. A pre-measured reference spectra in a know medium, e.g. water, is multiplied by a correction factor simulated through mode calculations, to yield the baseline associated with this medium. Our correction algorithm can be adapted to any analyte without knowledge of their characteristics, only requiring the refractive index of the solution. It also does not require any real-time calculation as the correction factor, depending on the refractive index, can be stored in a look-up table.

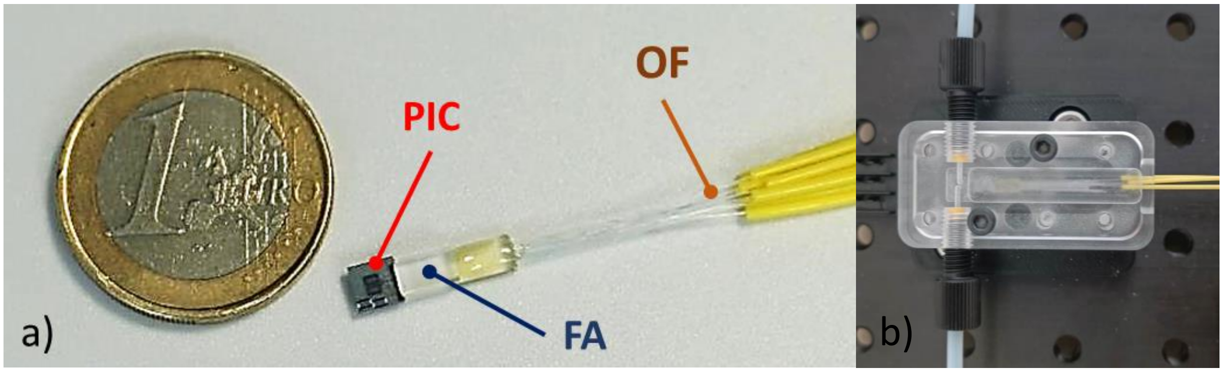

Figure 1: a) Photography of a packaged WERS sensor. OF: Optical fibres; FA: Fibre array. b) Photography of a flow cell incorporating a packaged WERS sensor.

3. Monitoring of *p*-coumaric acid bioproduction

One of the potential applications of WERS sensors is the real-time, in-situ chemical monitoring of biochemical processes. These complex processes involving living organisms can be improved by the measurement and control of so-called critical process parameters that may include e.g. the temperature, pH, and concentrations of various chemicals. However, traditional process analytical technologies such as chromatography based on sampling do not provide the continuous measurements required to control and optimize such processes, while optical sensors such as free-space Raman face issues linked to their cost, size, and performance.

The bioproduction of *p*-coumaric acid (*p*-CA) was used to illustrate the ability of WERS sensors to provide real-time information about bioprocesses. *p*-CA is a *p*-hydroxycinnamic acid used as the entry point in the phenylpropanoid pathway. It is a precursor of a wide range of other valuable plant secondary metabolites such as other p-hydroxycinnamic acids, flavonoids, and lignin, with numerous applications in the food, pharmaceutical, and cosmetic industries. However, its production is hindered by its hydrophobicity and its antimicrobial properties, which limit its accumulation in the fermentation broth []. This can be solved by a continuous extraction which currently cannot be monitored continuously: the separation of phenolic compounds like *p*-CA by liquid chromatography typically requires analysis times between 30 and 60 minutes, along with a high capital investment, a complex installation, and experienced users.

Solutions with varying concentrations were measured to establish the limit of detection (LoD) and the root mean square error of prediction (RMSEP) of a partial least-square (PLS) model for detection of *p*-CA in water. The results shown on Fig. 2 indicate a LoD below 100 mg/L and a RMSEP of 61 mg/L. These LoD and RMSEP values lie well below the requirements for the monitoring of *p*-CA.

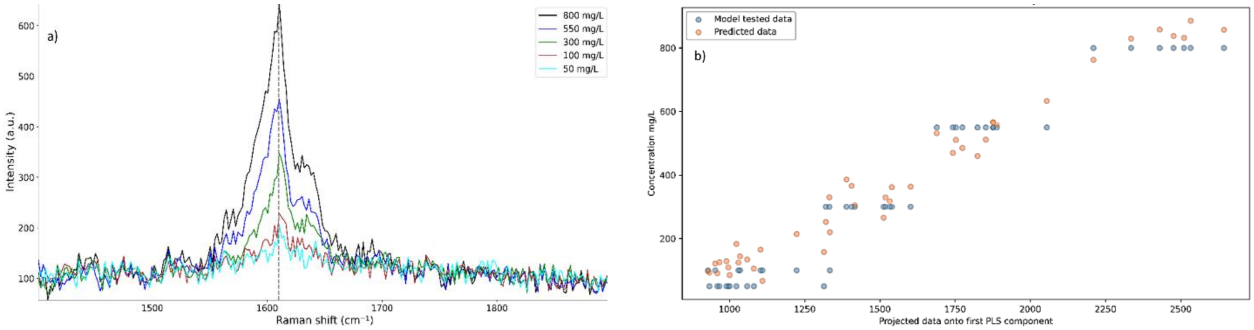

Figure 2: a) Background-corrected spectrum of diluted solutions of *p*-CA in water, zoomed in around the characteristic pic of *p*-CA around 1600 cm-1. b) Validation of the PLS model for prediction of the *p*-CA concentration of unknown solutions.

4. Conclusion

In summary, Raman spectroscopy based on fibre-coupled WERS combines Raman spectroscopy with integrated photonics, allowing for miniaturization, enhanced sensitivity, and integration into various analytical systems. Thanks to integrated couplers on the chip the sensor efficiency is not impeded by the usage of optical fibres. We present the monitoring of *p*-coumaric acid in the context of bioproduction and show a limit of detection of below 100 mg/L. These results show the potential of WERS sensors for industrial bioprocess monitoring. Further improvements to the coupling and filtering of the sensors, as well as measurements in complex matrices, are ongoing.

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