

# FLOW-THROUGH MICROFLUIDIC DIGITAL IMPEDANCE DETECTION

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## ABSTRACT

A Teflon coated flow cell has been designed for detection of analyte concentration and liquid identification of solvents. An AC voltage is applied across the flow cell to generate a current that is displayed in real time and used in solvent analysis. Experimental methods include injecting different concentrations of analytes in a flow path and analyzing current peaks that result as analytes enter the cell. The method provides a highly sensitive solvent identification and an alternative to more expensive and UV-dependent microfluidic sensing of analytes.

## KEYWORDS

Microfluidic, impedance measurement, electrochemical cell, 2-[<sup>18</sup>F]fluoro-2-deoxy-D-glucose ([<sup>18</sup>F]FDG), positron emission tomography (PET), high-performance liquid chromatography (HPLC), analyte detection

## INTRODUCTION

A simple, sensitive and inexpensive method for performing impedance sensing for analyte detection, liquid identification and water concentrations of solvents in microfluidic devices is presented. This novel platform builds on the principle of detection of precise volumes and droplet composition which has been demonstrated by other impedance measurement techniques[1–3].

## EXPERIMENT

AC voltage is applied across the flow-cell and the resulting current is digitized by monitoring the voltage drop across a series  $1\text{k}\Omega$  resistor. A software-based lock-in-amplifier matched to the input signal frequency improves sensitivity and the software displays the amplitude and phase of the current flowing across the cell in real-time (Fig.1). The flow-cell is a die-cut Teflon tape with  $9\ \mu\text{L}$  serpentine channel sandwiched between two Teflon coated electrodes (Fig.2). The device is based on the same serpentine electrochemical cell design as used in microfluidic synthesis of the positron emission tomography tracer 2-[<sup>18</sup>F]fluoro-2-deoxy-D-glucose ([<sup>18</sup>F]FDG)[4]. The main function of the previously reported electrochemical cell was solvent exchange of [<sup>18</sup>F]fluoride from aqueous to anhydrous organic media. However, the application of a recently developed signal analysis routine[5] and minimal hardware additions enabled real-time feedback information from the cell to characterize its contents. This affords valuable information such as the water concentration down to ppm concentrations (Fig.3), which can help optimize the performance of the electrochemical chip and determine when [<sup>18</sup>F]fluoride is dried to completion.

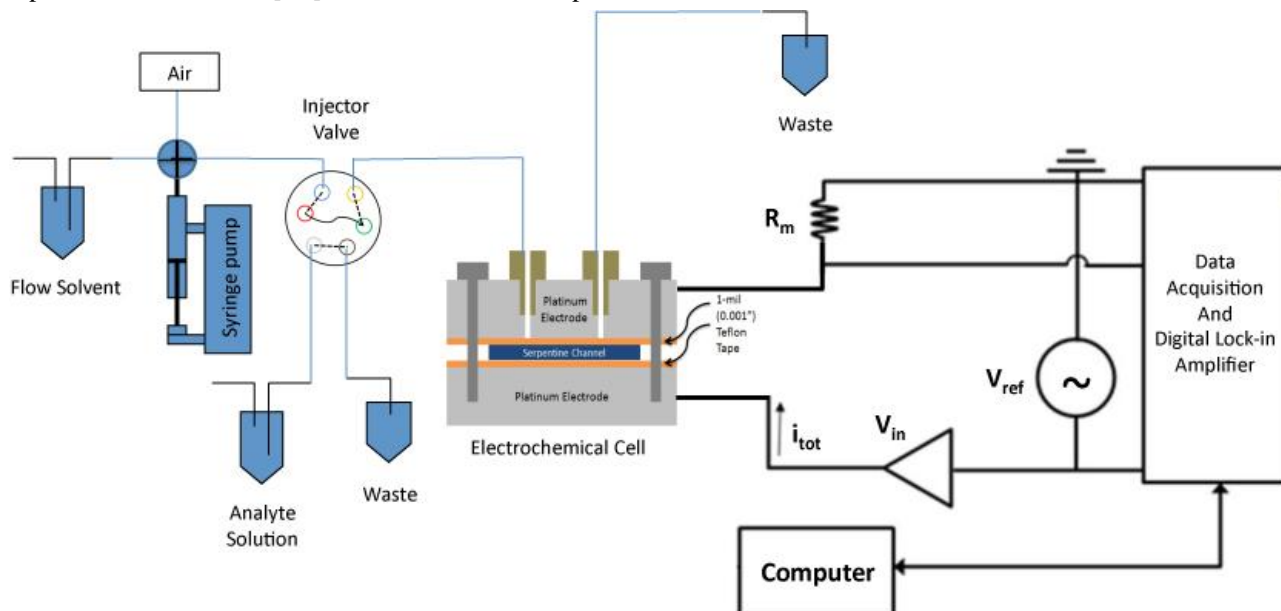


Figure 1 Schematic of digital impedance detection system

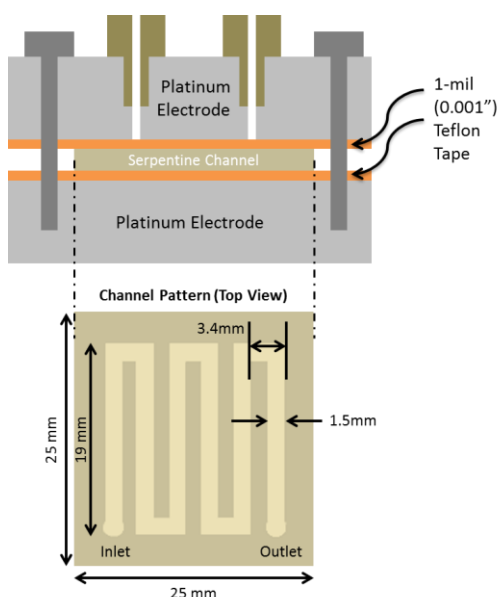


Figure 2 Impedance detection flow cell

Analytical experiments to determine the performance and sensitivity of the device were conducted by injecting 20  $\mu\text{L}$  of different concentrations of analytes into the flow path at constant flow rate of 10 mL/min. The current amplitude and phase were analyzed off-line and calibration was performed by calculating the integrals of resulting peaks as analytes passed through the chip. Experiments show that the cell is capable of quantifying the amount of water dissolved in MeCN down to at least the 100s of ppb level and the level of analytes pertinent to  $^{18}\text{F}$ FDG synthesis, such as  $\text{K}_2\text{CO}_3$ , Kryptofix-222, and mannose triflate at micromolar concentrations (Fig.4).

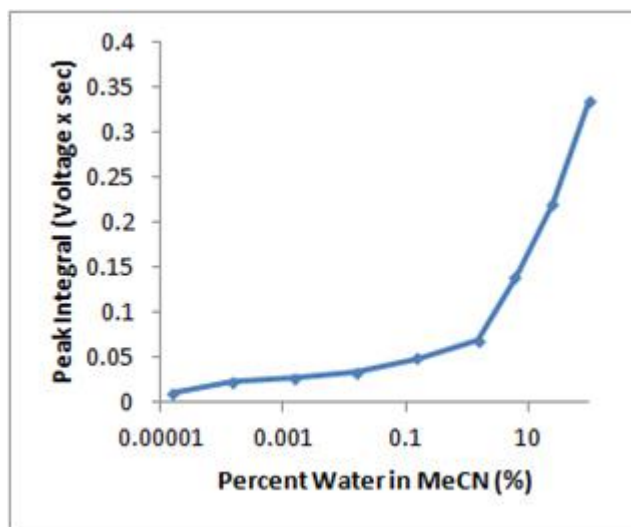


Figure 3 Impedance response of solutions with different concentrations of water in MeCN

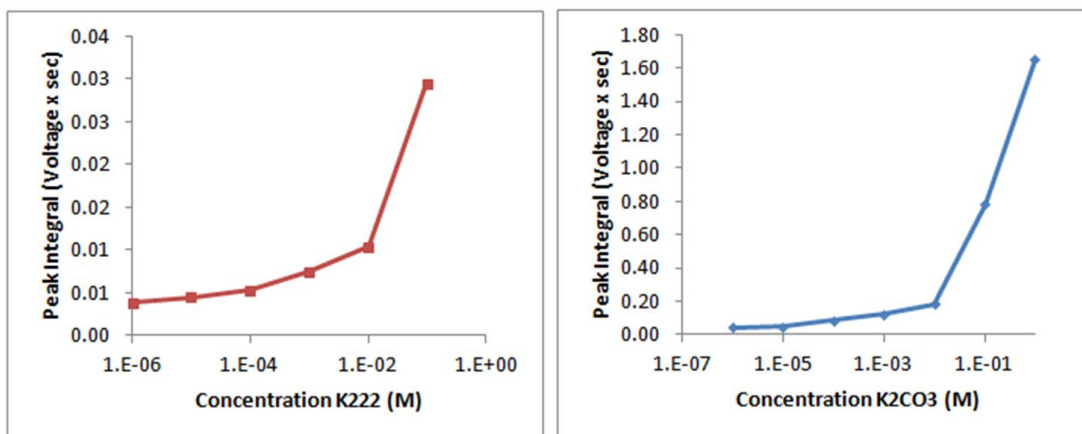


Figure 2 Impedance response of solutions with different concentrations of water in MeCN

The device's high sensitivity and ability to detect analytes without significant UV absorption (such as  $^{18}\text{F}$ FDG), enables the flow cell to serve as a detector added onto other microfluidic platforms or HPLC systems used in quality control of radiotracers produced for PET studies[6]. In a proof-of-concept experiment, the impedance cell and digital lock-in amplifier setup was placed in series with the HPLC column and UV and gamma detectors, and successfully detected the tracer  $^{18}\text{F}$ FHBG at the same retention time (Fig.5). Furthermore, detection of non UV absorbing molecules such as mannose triflate (Fig.6), suggests that 2-fluoro-2-deoxy-D-glucose could be detected and used for online specific activity measurement of probes such as  $^{18}\text{F}$ FDG produced in small amounts on microfluidic platforms.

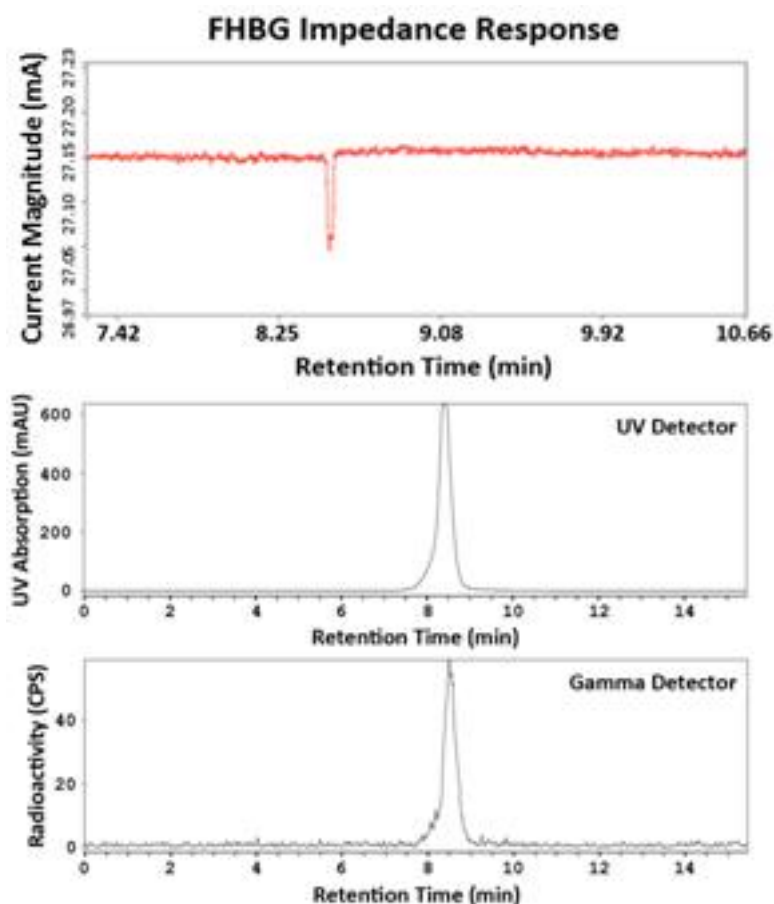


Figure 5 Impedance response of 0.001M FHBG after HPLC separation (Top) compared with response from UV and gamma detectors (Middle and bottom respectively)

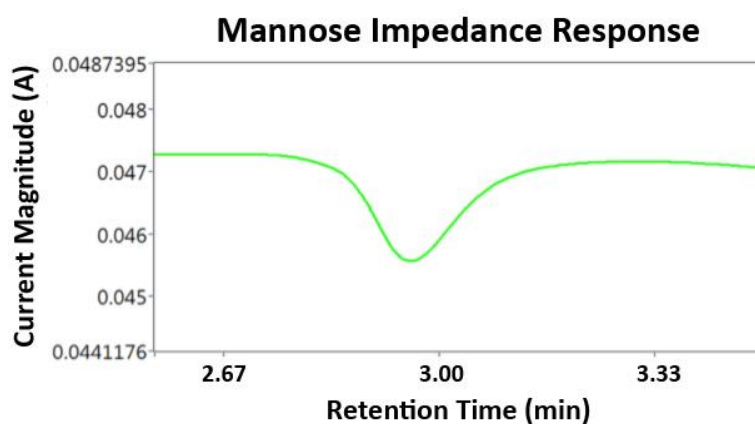


Figure 6 Impedance response for 1.0 mM mannose triflate sample injected into HPLC (flow rate: 1ml/min, mobile phase: 80/20 MeCN/H<sub>2</sub>O, column: C18)

Whether used as a standalone device for the detection of concentration of analytes in microfluidic platforms, in tandem with electrochemical solvent exchange to determine successful removal of water down to ppm levels or in conjunction with existing HPLC separation and detection systems, the impedance cell provides a versatile, inexpensive, and effective method for real-time chemical composition analysis during microfluidic processes.

## REFERENCES

- [1] S. C. C. Shih, R. Fobel, P. Kumar, and A. R. Wheeler, *Lab Chip*, Vol. 11, pp. 535–540, 2011.
- [2] M. J. Schertzer, R. Ben-Mrad, and P. E. Sullivan, *Sensors and Actuators B*: vol. 145, no. 1, pp. 340–347, 2010.
- [3] J. Gong and C.-J. Kim, *Lab Chip*, vol. 8, pp. 898–906, 2008.
- [4] S. Sadeghi, J. Ly, Y. Deng, and R. M. van Dam, *Proceedings of uTAS*, Groningen, 2010, pp. 318–320.
- [5] S. Sadeghi, *et. al* , *Anal. Chem.*, vol. 84, no. 4, pp. 1915–1923, 2012.
- [6] P. Y. Keng, *et. al* , *PNAS*, vol. 109, no. 3, pp. 690–695, 2012.

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