Laser manufacturing for multi-analyte paper-based diagnostic sensors

Ioannis N. Katis, Peijun J. W. He, Robert W. Eason and Collin L. Sones

Optoelectronics Research Centre, University of Southampton, Highfield, Southampton, SO17 1BJ, U.K.

Paper-based point-of-care diagnostic devices have been developing rapidly over the past few years since there is an ever-present need for affordable and reliable devices for medical monitoring that operate with minimal sample volumes, and hence devices that are portable and do not require special training or equipment for their use are very attractive. In developing countries especially, such devices are promising as they can enable revolutionary changes in the health sector by helping millions of patients through early-stage non-invasive clinical detection and diagnosis, which is in many cases extremely crucial [1].

We present here our work on the fabrication of paper-based multi-analyte diagnostic sensors for the detection of glucose and bovine serum albumin (BSA) using lasers-based methods. Our use of lasers for the fabrication of these devices is motivated by the versatility, speed of production, and cost, all of which are of critical importance for mass-market applications.

A laser direct-write additive process, Laser-Induced Forward Transfer (LIFT), much explored for depositing materials from a thin donor film onto a *receiver* substrate, was used to print (Fig. 1) the reagents/biological molecules that facilitate the sensing of the specific analytes [2] on the (cellulose) paper. The reagents LIFT-printed for the detection of BSA and glucose were tetrabromophenol blue (TBPB) and Glucose Oxidase/Peroxidase respectively. Prior to LIFT-printing, these reagent solutions were first spread using a wire coater on a quartz glass slide. This *carrier* slide was pre-coated with gold that acts as a Dynamic Release Layer (DRL). The DRL is essential for protecting the reagents from being degraded by the energy of the incident laser pulse by providing an opaque layer within which the laser energy gets absorbed and results in the propulsion (i.e. LIFT-printing) of the reagents onto the paper-receiver.

A second laser-based process was also used to create hydrophobic barrier-walls in paper substrates thereby defining the fluidic patterns shaped as wells or channels that can contain and guide biological and chemical solutions through the paper devices [3]. These channels and wells that contain and guide the reagents and the samples are critical for the implementation of multiplexed diagnostic devices, wherein the solutions need to be kept separate to avoid cross-contamination and false results. This writing process involves the impregnation of the paper substrate with a photopolymer, its illumination with the laser light at specific locations and its subsequent immersion in a solvent solution to remove any non-polymerised material. As shown on Fig. 2, this laser-based paper-patterning process does not inhibit the detection of BSA or glucose and is therefore ideal for the fabrication of such diagnostic devices.

A pulsed KrF Excimer laser operating at 248 nm was used for LIFT-printing and a continuous wave laser at 405 nm was used for the laser-patterning of the paper. The small dimensions of the structures patterned (~100 μm) and the precise and small-volume (nl) deposition of materials by these two processes enable the miniaturisation of these devices, thus ensuring the requirements for minimal use of expensive reagent and sample volumes. We have quantified the speed and cost of our laser-based methods and believe they can be up-scaled for mass production, as would be required for the future commercialisation of such a device.

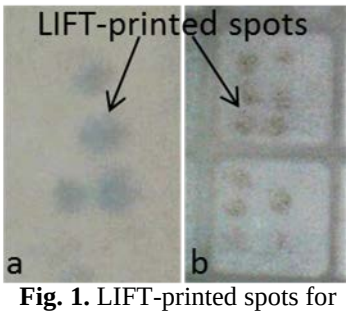

Fig. 1. LIFT-printed spots for the detection of (a) BSA and (b) glucose

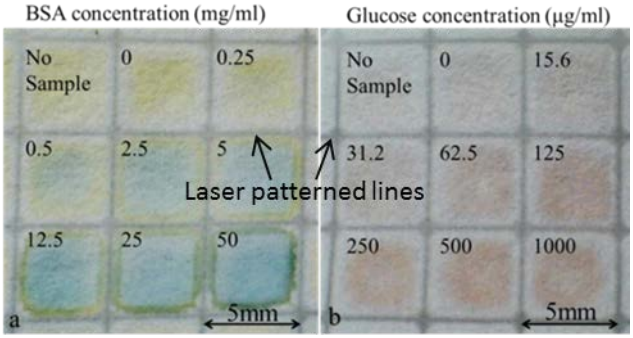

Fig. 2. Patterned cellulose paper for the detection of (a) BSA and (b) glucose, showing different concentrations of the analytes

References

[1] A. W. Martinez, S. T. Phillips, G. M. Whitesides, and E. Carrilho, "Diagnostics for the Developing World: Microfluidic Paper-Based Analytical Devices," *Analytical Chemistry*, vol. 82, pp. 3-10, Jan 2010.

[2] I. N. Katis, J. A. Holloway, J. Madsen, S. N. Faust, S. D. Garbis, P. J. S. Smith, *et al.*, "Paper-based colorimetric enzyme linked immunosorbent assay fabricated by laser induced forward transfer," *Biomicrofluidics*, vol. 8, p. 036502, May 2014.

[3] C. L. Sones, I. N. Katis, P. J. W. He, B. Mills, M. F. Namiq, P. Shardlow, *et al.*, "Laser-induced photo-polymerisation for creation of paper-based fluidic devices," *Lab on a Chip*, vol. 14, pp. 4567-4574, 2014.