3D printing in separation science: Hype or reality?

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Three-dimensional (3D) printing is an emerging and enabling technology that is paving its way in different fields of research, including analytical science, for the fabrication of custom devices and portable sensing platforms based on additive manufacturing of objects from CAD models. In fact, the last 5 years have witnessed tremendous advances in novel materials and composites with improved chemical properties (e.g, noble metals and chemically resistant polymers) and printing platforms for fabrication of low-cost devices capitalized on stereolithography (SLA) or dynamic light processing (DLP), inkjet printing, fused deposition modelling (FDM) and selective laser sintering (SLS) that enable decentralized measurements. The main advantages of 3D printing are the capability of rapid and single-step prototyping of holders, scaffolds, and integrated complex systems with geometries that cannot easily be manufactured by conventional means, such as computer numerical control milling and soft-lithographic approaches. Furthermore, the outreach of this technique has been recently expanded by the lowering costs of the machinery, the user friendliness of the CAD/CAM software and specially the commercial strategies addressed to the non-technical and non-scientific collective, currently called 'maker community'.

In the scientific sphere, a variety of 3D printing technologies including multi-material printing is now available in the market for the fabrication of cost-effective fluidic platforms for microscale sample preparation and column separation systems. Efforts toward designing unrivalled 3D printing structures have triggered the development of printable sorbent materials and membranes using either pristine or chemically modified polymers for on-line sorbent extraction/concentration, and platforms for chromatographic and even electrophoretic separation by using conductive printable materials. Also, 3D printing fostered a new dawn for flow injection analysis with the fabrication of versatile millifluidic platforms within the concept of "3D-printed μFIA". Recent literature in the field of 3D printing in separation science aiming at the so-called "Office Chromatography" focused on the (i) exploration of chromatographic features of tailorable 3D-printed HPLC column geometry with complex designs, (ii) feasibility of *in-situ* fabrication of covalently-attached porous organic monoliths into 3D printed polymeric or metal scaffolds, and (iii) cost-effective fabrication of printed thin layer chromatographic plates and entire gel-

electrophoresis setups. Current trends are also focused on the development of 3D-printed microchips with features <50 μm for on-line electrophoretic separation of peptides and proteins as biomarkers and the exploitation of multi-material polyjet-type printers for integration of membrane separation and electrokinetic separations on chip for clean-up and separation of pharmaceuticals.

However, 3D-printing in analytical science is still at its infancy because most of the applications reported in the literature are overly simplistic. In fact, the three main 3D-printing technologies (FDM, SLA/DLP and SLS) have a series of problems or disadvantages that must be solved before their acceptance and full integration in the analytical chemistry lab. For example, the use of FDM prints at relative high pressures (>15 bar) is troublesome and can only be achieved by expensive 3D printers. In the case of SLA, most of the photopolymerizable resins are proprietary, and custom-grade printers only accept resins provided by the manufacturer. In both cases, resolution of the 3D-printers does not suffice for truly microfluidic separations and tailor-made printer configurations with optimized laser sources and optical disposition is needed in SLA applications. Last but not least, post-printing curation is capital in 3D-printed SLA objects to prevent leaching of monomers or oligomers that might otherwise jeopardise the analytical detection step, in particular when coupled to mass spectrometric detection. In the case of SLS, the available instruments are still too expensive for being incorporated as a common instrument in analytical research laboratories, and the resolution and features are still at similar levels than those of SLA/DLP machines. Similar to SLA, post-printing steps are necessary in SLS for removal of the non-sintered metal from the channels, which is not a straightforward task. In this context, the high printing precision achieved by the two-photon polymerization technique where sub-micron features can be fabricated is worth mentioning. However, the high cost, tedious workflow and small printer area are still the main challenges of this cutting-edge technique.

In brief, 3D printing in analytical science has been mostly used in proof-of-concept studies or disposable platforms, and no application to complex matrices (wastewaters, whole blood or industrial samples) has been demonstrated as of yet. At this juncture, we can conclude that 3D printing is still a hype in analytical science yet this technique is proven to outperform conventional techniques in terms of flexibility in fabrication of unique and singular designs. We anticipate that 3D printing will become a standard technique for prototyping in most R+D laboratories when inert materials will be printable at low cost. Apart from the mainstream printers targeting to a wider market, other technically oriented approaches will become key players for further development of 3D printing, such as the usage of electronic components or chemically active materials inside of the prints or the elimination of the post-printing procedures for a truly single step fabrication.