

### 3D Printing of Porous Media at the Microstructural Scale

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What is superficially referred to as ‘packing quality’, a myriad of geometrical parameters governing the interrelations between pores, has only been measured post-hoc in the form of separation efficiency. While several computational studies of chromatography bed microstructures have explored the effects of various packing parameters on dispersion, experimental replication and model validation has remained elusive. Additive manufacturing, or 3D printing, offers the opportunity to manufacture porous media composed of micro-structural elements of different shapes and sizes, and to precisely locate and orient them within the bed. For example, spherical beads with a narrow size distribution can be constructed individually at desired locations within the bed, allowing the creation of specific packing arrangements, i.e. perfectly ordered lattices or random packing mimicking conventionally packed chromatography columns. Further opportunities are to create geometric elements with different shapes or sizes and place them at individual locations within the same bed. Alternatively, the structural focus can shift from the solid-phase to the mobile phase, with the design of complex flow channels within a monolithic bed. These observations led us to propose the use of 3D printing as both a chromatography column production method and as a tool to enable fundamental studies of packed bed microstructures.

The main challenges to this approach include achieving sufficient printing resolution to compete with current media in terms of theoretical plate height and developing materials that have appropriate internal porosity and surface functionalities to enable high binding capacity and specificity. Other challenges are as for conventional media, for example good swelling properties, low non-specific adsorption, and the absence of toxicity and leaching.

Here, we show examples of progress made to date in creating 3D printed chromatography columns. These include i) micro-structural analyses of columns containing porous beds with a variety of lattice arrangements and channel structures, printed at a maximum current printing resolution of 16  $\mu\text{m}$  and ii) comparison of residence time distributions and flow characteristics for a range of columns, including several printed with different integrated flow distributors and column cross-sections. We demonstrate reasonable fidelity between printed and designed columns and identify current limitations with regard to resolution. Finally, we compare packed beds incorporating deliberately introduced imperfections within packing lattices, including a ‘line defect’ that runs the length of the column and a ‘cluster defect’ consisting of localized voids at various locations within the packing. Experimentally determined reduced plate heights are compared with computational fluid dynamics flow studies.