Downstream bioprocess characterisation within microfluidic devices

Miniaturising bioprocess unit operation steps is a well-established approach to find novel routes for process intensification and improved process economics. While a number of microbioreactors have been presented over the last 15 years, miniaturised downstream unit operations (mDUO) are less developed which has, to some extent, hindered their implementation as early process development tools. Microfluidic devices are particularly attractive for using fewer resources, for having the possibility of parallelisation and for requiring fewer mechanical manipulations. The expectation is that these devices will facilitate the rapid definition of critical process parameters, and thus ultimately reduce production costs.

We have developed several microfluidic mDUOs and combined them with advanced and novel analytical approaches, resulting in devices that can potentially be employed for both analytical and preparative purposes; these include devices for cross-flow filtration, liquid–liquid extraction and flocculation. To accelerate in-depth process characterisation, we developed and implemented on-line monitoring approaches and image-processing algorithms.

In this contribution, we will present results for the liquid–liquid extraction of pharmaceuticals, for the purification and concentration of drug delivery vehicles, and for the flocculation of yeast cells in microfluidic devices. For the latter, we will present for the first time the capability to study flocculation-growth independent from the floc breakage phase; two phases which are in a state of equilibrium in larger scale systems, and can thus not be discerned in conventional systems. The applicability of these devices will be shown with the assembly of a train of mDUO for the enzymatic production of chiral pharmaceutical intermediates.

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