A TRULY CONTINUOUS COUNTER-CURRENT DOWNSTREAM

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The current integrated and continuous bioprocessing (IBC) downstream is batch chromatography run quickly with multiple columns to make it appear continuous. This configuration is sub-optimal. The downstream technology has not improved radically in the last 20 years, with the possible exceptions of resin development achieving much higher capacities and selectivity, in-line solution formulation, and high capacity, low fouling membranes.

We propose a truly continuous downstream without chromatography, based on affinity tangential flow filtration. The affinity ligands used will be described in detail. We have achieved a proof of concept for each stage of the mAb downstream. The downstream achieves acceptable levels of HCP and DNA, as well as reduces the Process Mass Intensity from 3000 kg water per kg drug to below 1000. As a result of the decreased water use, the purification equipment is significantly smaller.

Everything required for this downstream exists, and we believe the process could be made commercially viable as it stands. The process could be improved significantly, though. We map out possible modifications to achieve a PMI below 300. Much work is required from vendors and academics to optimize the membranes and affinity ligands, as well as from vendors to make a new kind of integrated continuous downstream equipment.
The goal of this talk is to create a new global platform based on radically new vision for the downstream. This vision is disruptive: for instance, it effectively ends the commercial Protein A resin market. The vision also includes multiple redundancies for supply chain, including in-house 3D printing of single use equipment