NOVEL SINGLE-COLUMN SIMULATED MOVING-BED CHROMATOGRAPHY FOR QUASI-CONTINUOUS BIOPURIFICATION

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Liquid chromatography is currently the core technique for purification of biopharmaceuticals, and its use is often integrated vertically within the downstream processing (DSP) strategy, as it easily fits into the early capture stage as well as into the final purification phase. Single-column batch chromatography, which because of its simplicity is routinely used by industry, isolates the pure part of the product peak one is interested in at the expense of yield because the impure side fractions, containing valuable product, must be discarded. Multicolumn continuous chromatography, whose most efficient implementation is based on the simulated moving-bed (SMB) concept, captures the side fractions by internal recycling until the entire product has been extracted while new feed is continuously or cyclically injected. This not only gives significantly higher yields of purer product, but also enables you to process more feed and thereby increase overall throughput.

We have developed a new chromatographic platform based on a novel single-column device that mimics the operation of multicolumn chromatography through ingenious management and recycling of mixed fractions. The newly developed platform shares the benefits of SMB chromatography in that it not only gives significantly higher yields of purer product, but also enables processing more feed and thereby increasing the overall throughput. However, our process uses a single chromatographic column.

The new process is based on the realization that the periodic state of an SMB process can be mimicked by a single-column chromatographic process with a recycle lag of $(N-1)\tau$ time units, where N is the number of columns of the equivalent SMB unit and τ is the switching interval (time interval between consecutive switches of the inlet and outlet ports). The recycle lag is implemented in practice by means of a special type of plug-flow tube that includes a moving piston to compensate for the difference between inlet and outlet flow rates. The proper operation of the inlets and outlets of such device implements an approximate “first in, first out” method for organizing and manipulating the fractions of fluid collected from the chromatography column, where the oldest (first) amount fluid, or ‘head’ of the fraction, is the first to exit the plug-flow tube.

It is shown that the single-column chromatograph can mimic the operation and performance of recent multicolumn capture and polish processes designed for the efficient separation and purification of monoclonal antibodies, biosimilars, and viral vectors. Moreover, the single-column chromatograph can be easily integrated into the existing downstream processing platforms of complex biopharmaceuticals.