HP-RFC - Radial Flow Chromatography

A. High throughput

Fig. 1. The bleed-Outlet (i/q) ratio (i) is the most important parameter responsible for the differences between axial and radial processing. During scaling-up, this parameter is leading. In HPRFC a i/q is considered default.

Fig. 2. A lower pressure drop, flow focusing

B. Lower pressure drop, flow focusing

Compared to axial, radial process columns result in a lower pressure drop at equal bed height. The pressure drop (ΔP) is the sum of resistance of the packed bed and pre- and post filter. The cylindrical shape of the filters in the radial design allows the filters to be utilized in a highly porous, even at process scale operation. Filter resistance is the main attribute responsible for a lower pressure drop in radial columns.

Pressure drop (ΔP) through a packed bed is explained by the Kozeny-Carman equation: the increased friction by the increased superficial velocity at the exit of the column causes extra resistance, especially responsible for flow focussing. An average ΔP in the packed bed of the "heated" bed is 40% at ΔP dropping to 21%. The added resistance at increasing axial axes is responsible for the even flow distribution in large/taller short bed height process columns and is crucial for crude feed applications like expressed in TRACK2.

C. Effect of increasing the α-value on column geometry

Increasing α-value will also result in smaller footprint and taller columns at equal bed-height and volume. Reduction of footprint, improved handling and reduced CapEx are appreciated. Sometimes concerns are raised about gravity compression of soft type media in taller columns.

Table 1. Effect of α-value on column geometry, volume and weight on equal bed height

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D. Buffer/Slid/Skid/Operator column

3D Flow modelling is used to determine proper distribution of the process liquids during processing.

As demonstrated in the model in figure 2, the distribution chamber of the 3D-center inlet is effective to support even distribution. In the event uneven distribution is shown, without increasing the size of the chamber, flow distribution can be optimized before the design is finalized for release for manufacturing.

Cleanroom footprint reduction & compatibility with disposable-bag buffer-totes

Implementing HP-RFC columns will result in significant cleanroom efficiency improvement and often enables flexible cleanroom use. Process columns up to 1,000 kg can be executed with casets, but even the larger columns (B01) remain relatively mobile.

An Axial column of B01, with a bed height of 20m will have a footprint of ~7.5m², whilst its Radial counterpart only occupies just 3.0m² (38%) (Table 1). Increasing production capacity in a relatively small cleanroom and/or more efficient use of the equipment can be achieved. The reduced space requirement supports the use of disposables/bag buffer-totes. Reduced risk of injury in maneuvering buffer-totes is a clear advantage of the extra available space.

Introduction

Are Axial and Radial flow chromatography different? [1]. Demonstrated by multiple comparative studies over the last 2 decades and further corroborated in mathematical modelling studies done by J. Research (University of Wageningen), chromatographic performance is found to be “not different.”

The study additionally provided valuable insight to fundamental parameters that were applied to tune design-choices supporting linear scale-up over a broad range. In this paper the attributes that make the axial and radial columns differ at the operational level (column mobility, higher throughput, process robustness, effortless packing and efficient use of cleanroom space) are addressed by the example of a scale-up from lab-bench to a 600 liter column scale, a scale-up factor of 1:30,000.

Table: Scale up

Proxys Micro columns - Scale-up/scale-down tools

Small scale Micro-RFC columns are tubular columns designed to explore Radial Flow Chromatography and effectively micropack larger radial process units at small volumes. Ideal for initial development or scaling down for virus clearance studies. Micro-RFC columns are available with bed heights starting at 7 cm up to 28 cm. Packing principle is closely compatible to the packing of the larger columns and therefore results compare as well. Pre-packed, pre-assembled columns are available for all sizes.

Proven Linear scalability, 1:30,000

4001, Tripel + ES-Pack QS08HT

Recently Proxsys completed the world’s largest Radial Flow Chromatography column. The Tripel 4001, features a hydraulic Triplet lifting mechanism for packing port operation as well as column maintenance. The ES-Pack QS08HT packing station, equipped with Quatroflow 2DR, is designed to automatically pack the column. The load-program Quatroflow 2DR is programmed for continuous flow or continuous pressure-packing to achieve the predetermined bed compression from an optimized recipe. These ensure reproducible results for each packing. Automated unpacking is achieved with minimal dilution.

Flow distribution, fit architecture & its resistance, bed height, column hydrodynamics and all other physical parameters are maintained from small scale columns up to a full radial column. Chromatographic results achieved in small scale radial microm columns are very close to that of full radial process columns, making the Proxys Radical column technology truly linear scalable.

Thanks to the patented annular packing port, the packing of any HP-RFC column is scalable, reproducible, effortless and typically takes about 10 to 30 minutes irrespectively the column size.

Linear scalable from 20m lab scale (nominal) to 4000 industrial process size

Conclusion

A. Higher overall results in a shift of the crossover point and thus equips positive on mass transfer and throughput. Throughput can be increased without loss in binding capacity

B. Increasing the oval will increase pressure drop over the radial bed, at shorter bed-Heights and/or larger head sizes this improved distribution by flow focusing.

C. The flow focusing is the main driving force for the exceptional suitability of RFC columns for crude feed processing in TRACK applications.

D. Without erosion in performance, increasing the oval will make the RFC columns more compact. Weight, space requirement, CapEx as well as DoE’s are reduced, while mobility is increased.

References:

[1] Are axial and radial flow chromatography different? J. Research (University of Wageningen), chromatographic performance is found to be “not different.”


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(downstream bioreactors)