Alluvial Filtration – An Economical Solution for Midstream Clarification

Introduction

Continuous process optimization is a key factor in the biotech industry. With higher particle loads (>108 cells/ml), standard technologies for cell removal (midstream processing) – e.g. centrifugation, separation, membrane- and depth filtration – find their limits.
To increase efficiency and making the midstream process more economical alluvial filtration is the state-of-the-art solution. Alluvial filtration is a type of depth filtration and a well-established, economical method in pharmaceutical industries (e.g. plasma fractionation). Instead of using an immobilized depth filter medium, filter aid (e.g. diatomaceous earth, perlite) is used to constantly build a filter cake during filtration. The filter cake with its resistance acts then as the actual filter medium. Alluvial filtration, therefore, leads to a higher filter capacity – especially with compressible particles, e.g. microbial or mammalian cells. This technology leads to a maximum product yield and highest economic efficiency and is linear scalable from lab to production scale.

Midstream, the (missing) link between up- and downstream

The removal of cells and cell debris are process steps between upstream processing (fermentation) and downstream processing (purification). These intermediate process steps are being referred to as midstream processing (Fig. 1). Midstream processing is often done by a combination of several operation units. A highly efficient method is alluvial filtration which can be done with FILTRODISC™ BIO SD. Midstream processing is amongst the most important step in biotech processes. Nowadays, cell culture systems are the method of choice to produce therapeutics and diagnostics. For this purpose, the use of mammalian cells is predominant, but also bacteria, yeast and insect cells are being used. Involved in the process design for the right cell removal system are questions about: process efficiency, process robustness, economic feasibility, as well as legal aspects. Challenges for process efficiency are higher and higher cell titers, amount of cell debris, scalability, robustness and flexibility in terms of process changes and future process adaptations and process optimizations. The industry asks for more efficient and economic methods.

Seed train *Bioreactor* *Several Chromatography* *UF/DF*

Filtration in only one step

FILTRODSIC™ BIO SD is the first micro filtration system, which combines the advantages of standard depth filtration and alluvial filtration in a single-use system, resulting in new possibilities for midstream processing and subsequent downstream processing steps. Instead of a two-step cell removal system with centrifuges and depth filters, just one step is necessary to remove cells and cell debris from a fermentation broth. The centrifugation step can be eliminated.
The product range start with a 2" capsule for development work for up to 1 l fermentation broth. Followed by a 5" capsule for up to 10 l and a 10" capsule for up 25 l. All this are standalone systems (Fig. 2).

Fig. 2: 2", 5" and 10" capsule

For the scale up into pilot and production scale lenticular modules with a surrounding bag are used. For use of these modules a support housing is necessary. The starting volume is around 100 l and is scalable up to 1000 l for one module. For bigger scales a combination, also automated, of several modules is possible.

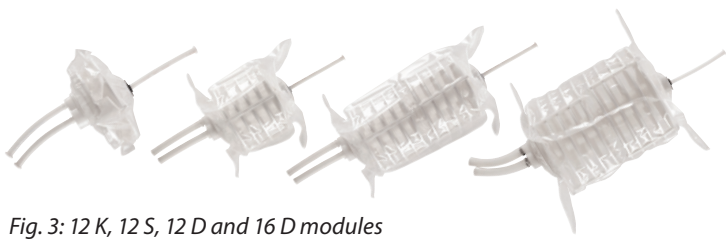

Fig. 3: 12 K, 12 S, 12 D and 16 D modules

Fig. 4: DISCSTAR 12K, DISCSTAR 12D and fully automated DISCSTAR 16D double housing

Scalability

FILTRODISC™ BIO SD is linear scalable from lab to production. The cake volume per liter of filtered liquid, determined during lab trials with the 2" capsule, is directly proportional to the cake volume needed for the production scale filter modules. This shows that the primary focus when working with alluvial filtration is not on the scale-up calculation of the filter area, but the required cake volume. the FILTRODISC™ BIO SD system can also decrease impurity levels, e.g. DNA or HCP, which leads to cost reduction in the subsequent chromatography steps.

More information needed: Please visit our website (https://www.filtrox.com/applications/filtration-for-life-science/bio-sd/) or contact your next FILTROX office (https://www.filtrox.com/contact-us/locations/)

Ralph Daumke, Global Market Manager Life Science, FILTROX Group
applications@filtrox.com, www.filtrox.ch