Membrane separations: range of options

M. Estabrook and M. Beauchemin
Amersham Biosciences, Membrane Separations, Westborough, MA, USA

Purification of biomolecules using membrane separation technologies is an integral component of many purification strategies. Amersham Biosciences offers two classes of cross-flow membrane separation products, flat sheet membrane cassettes and hollow fiber cartridges. The products and processes scale predictably from the lab bench to pilot scale to production. This article summarizes the range of membrane separations products available from Amersham Biosciences.

Introduction

The purification of biological therapeutics—indeed, purification in many bioprocessing domains—generally utilizes both membrane separations and chromatography (Fig 1).

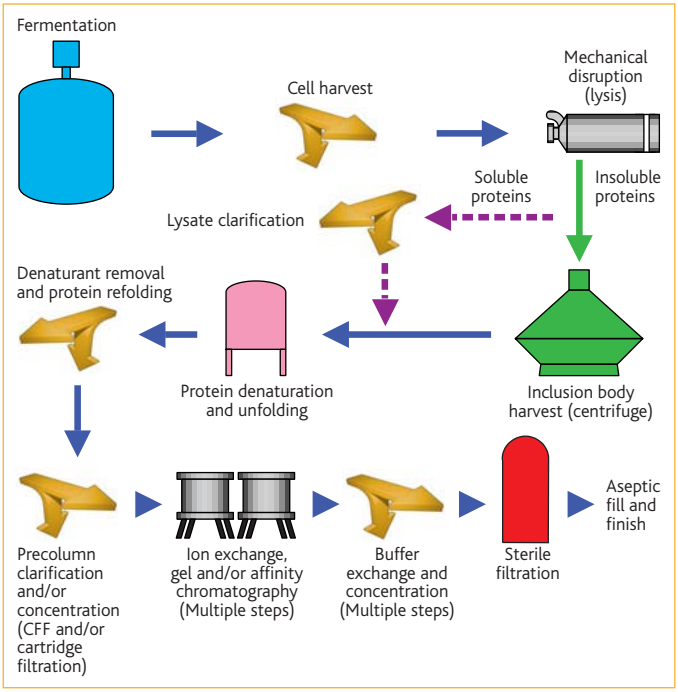

Fig 1. Purification by cross-flow membrane separation is integral to the manufacture of biological therapeutics. Membrane separation steps are depicted as bi-directional yellow arrows in this flowchart of a typical purification procedure for a recombinant protein.

Chromatography offers greater selectivity than membrane separations, and can purify large quantities of solution in one operation. Yet, in both primary and downstream processes, membrane separation technologies offer a number of key benefits. They are fast, robust, and can bring greater effectiveness to the following stages of processing (e.g. by concentrating and washing feedstreams prior to chromatography).

Membrane separation products

Amersham Biosciences designs, manufactures, and markets two classes of membrane separations products, flat sheet membrane cassettes and hollow fiber cartridges. The recently introduced Kvick™ Cassettes are flat sheet membrane cassettes that feature a zero dead space design, high selectivity, sharp cutoff, and minimum hold-up volume. The cassettes are constructed using low-extractable materials.

Hollow fiber cartridges are available for both cross-flow microfiltration and ultrafiltration separations processes. Hollow fiber cartridges are best known for their open feed-stream paths, and their ability to process cell cultures without compromising mammalian cell viability.

Both the cartridge and cassette designs permit high membrane packing density, and both can be scaled predictably from laboratory to production volumes.

How cross-flow membranes work

Amersham Biosciences separations cassettes and cartridges are designed for cross-flow (tangential flow) operation. Unlike single pass or dead-ended filtration, cross-flow methodology continuously sweeps the membrane surface, recirculating the feedstream across the membrane. Doing so minimizes clogging membrane pores (blinding) and promotes consistent, long-term productivity. Cross-flow also allows units to be cleaned, stored, and re-used as needed.

With cross-flow membranes, as the feed stream is pumped through the cassette or cartridge, the retentate—the materials excluded by the membrane pores—continues through the recirculation loop, while the permeate, including solvent and solutes, is transported through the membrane pores and collected separately (Fig 2).

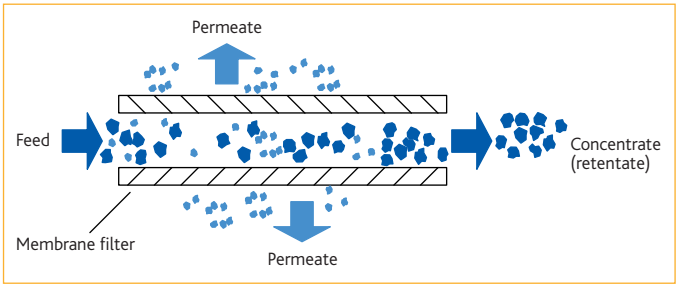

Fig 2. The principal of cross-flow filtration. Molecules smaller than the cutoff weight of the membrane pass through the membrane as the permeate. Larger molecules, excluded by the membrane pores, are retained and concentrated.

Kvick cassettes

The Kvick cassettes (Fig 3) integrate a new internal design with materials that exhibit very low extractables. The membranes are precise and reproducibly selective, with sharp cutoffs. The innovative, patent pending anti-dead space design optimizes the efficiency of fluid flow and ensures that solutions reach all of the membrane surface area. This minimizes the risk of cross contamination and the potential of product loss in dead space surface area. Fluid paths are consistent across both Kvick Lab and Kvick Flow Cassettes, allowing linear scale-up. An integrated gasket precludes the need to install separate gaskets between cassettes.

Kvick Lab Cassettes are available with 0.01 and 0.12 m^2 (0.1 and 1.25 ft^2) membrane areas. The larger, Kvick Flow Cassettes are available in 0.46 and 2.33 m^2 (5 and 25 ft^2) membrane areas. Currently, both Lab and Flow cassettes are available in 10 000, 30 000, 50 000, and 100 000 nominal molecular weight cutoffs (NMWC).

Kvick cassette systems

The Kvick cassette family of systems includes both a lab cross-flow system (Kvick Lab) and a pilot-to-production scale system (Kvick Flow) (Fig 4).

Fig 3. Kvick lab and Kvick flow cassettes are available in a variety of membrane areas and molecular weight cutoffs to fit almost any application.

Kvick Lab Separation System (Fig 4A) can hold up to five Kvick Lab Cassettes, and includes a 2.5 liter reservoir, rotary lobe pump, pressure gauges, and necessary valving, piping, connectors, and fittings. The lab system can concentrate product volumes as low as 200 ml. Installable membrane area ranges from 0.1 to 0.58 m^2 (1–6.25 ft^2).

A

B

Fig 4. Kvick cassette systems are available in bench-top (A) and pilot/production scale systems (B).

Kvick Flow System for pilot/process scale operations (Fig 4B) is designed for 5–1000 liter batches, and includes a rotary lobe pump with protection against over-pressure, full-size Kvick Flow Cassette Holder, reservoir, and necessary valving, piping, connectors, and fittings. The system accommodates up to 10 Kvick Flow Cassettes with an installable membrane area from 0.46 to 4.6 m^2 (5–50 ft^2).

Cartridges

Amersham Biosciences offers more than 20 different cartridge designs, 10 ultrafiltration (UF) ratings, four microfiltration (MF) ratings, and six hollow fiber lumen diameters (Fig 5).

Fig 5. Cartridge designs accommodate lab to production volumes. Pictured, from left to right are lab-scale cartridges MidGee Hoop, MidGee, and Xampler; pilot-scale cartridge sizes 5, 6, and 9; process-scale cartridge size 55, and Maxcell cartridge.

MidGee™ and MidGee Hoop™ Cross-Flow Filters are designed for rapid laboratory concentration and/or diafiltration of critical biological solution volumes up to 200 ml. They offer the convenience and speed impossible to achieve using stirred cells or dialysis tubing in various cross-flow configurations for linear scale-up. MidGee cartridges offer high product recovery with minimal shear denaturation. UF pore sizes are 1000–500 000 NMWC, while MF pore sizes are 0.1–0.65 µm.

Xampler™ Laboratory Cartridges enable rapid concentration and/or diafiltration of critical biological solutions up to 5 liters, with membrane areas from 110 cm^2 to 1400 cm^2. The cartridges are autoclavable.

Pilot Scale Cartridges allow rapid concentration and/or diafiltration of critical biological solutions up to 100 liters with membrane areas ranging from 0.12 m^2 to 1.15 m^2.

Process Scale Cartridges provide the greatest possible membrane area for a given size, with up to 28 m^2 of membrane surface area in a single device. Steam-in-Place Cartridges that are capable of withstanding multiple SIP cycles for aseptic processing are also available. Maxcell and Procell™ Large Process Scale Cartridges are specifically designed for biomanufacturing operations for rapid concentration and/or diafiltration of critical biological solutions from 50 to 1000 liters.

Cartridge systems

Amersham Biosciences also provides a range of cartridge-based systems, from small systems for laboratory scale to larger scale systems that are modular in design.

MidJet™ Systems are compact and self-contained, using MidGee Cross-Flow Filters to facilitate rapid processing of volumes up to 200 ml. Low hold-up volume allows concentration of volumes as small as 2–5 ml.

QuixStand™ Basic Systems are compact, self-contained units designed for Xampler laboratory cartridges for rapid processing of volumes up to 10 liters, and linear scale up from pilot- to process-scale. Through an available peristaltic or rotary lobe pump, a QuixStand system can be pressurized for continuous diafiltration or gentle recirculation of sensitive solutions.

FlexStand™ Systems are modular systems designed to accommodate pilot scale cartridges from 0.12 m^2 to 3.25 m^2 for volumes from 5 to 100 liters and more. GrandStand™ Process Systems are self-contained and designed for MaxCell™ Process Scale cartridges up to 13 m^2. Process volumes range from 50 to 1000 liters and higher. Grandstand systems can be controlled by the same UNICORN™ control software used on ÄKTA™design and BioProcess chromatography systems.

Broad range of experience

Offering one of the widest ranges of cross-flow membrane products available on the market, Amersham Biosciences can help shorten development time by providing the cartridge design and system to match specific application needs.

The combination of proven chromatography products with advanced membrane separations products provides a well-mapped path for a large variety of bioprocessing needs. The range of services and products, including biosafety, Fast Trak™ Education, and custom products, enables Amersham Biosciences to supply the downstream solutions necessary to support the development and manufacture of biopharmaceuticals.

Ordering Information	
Kvick Lab Cassette, 10 000 NMWC, 0.01 m^2, standard	56-4112-04 (UFELA0010001ST)
Kvick Lab Cassette, 10 000 NMWC, 0.01 m^2, select*	56-4112-06 (UFELA0010001SE)
Kvick Lab Cassette, 30 000 NMWC, 0.01 m^2, standard	56-4112-08 (UFELA0030001ST)
Kvick Lab Cassette, 50 000 NMWC, 0.01 m^2, standard	56-4112-10 (UFELA0050001ST)
Kvick Lab Cassette, 100 000 NMWC, 0.01 m^2, standard	56-4112-14 (UFELA0100001ST)
Kvick Lab Cassette, 10 000 NMWC, 0.12 m^2, standard	56-4113-25 (UFELA0010010ST)
Kvick Lab Cassette, 10 000 NMWC, 0.12 m^2, select*	56-4113-26 (UFELA0010010SE)
Kvick Lab Cassette, 30 000 NMWC, 0.12 m^2, standard	56-4113-27 (UFELA0030010ST)
Kvick Lab Cassette, 50 000 NMWC, 0.12 m^2, standard	56-4113-28 (UFELA0050010ST)
Kvick Lab Cassette, 100 000 NMWC, 0.12 m^2, standard	56-4113-29 (UFELA0100010ST)
Kvick Lab Cassette Holder	56-4112-79 (KLHR0105000SS)
Kvick Lab System (115 VAC)	56-4112-77 (KLSY0105RLPSS15)
Kvick Lab System (220 VAC)	56-4112-78 (KLSY0105RLPSS20)

**Particularly effective for recombinant proteins.*

The table above is a select list of catalog numbers for the Kvick family of products. Please visit www.bioprocess.amershambiosciences.com for a complete list of the Kvick family of products and to obtain the new Hollow Fiber Selection Guide.