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A laterally-fed membrane chromatography module

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ABSTRACT

Module design is of critical importance in membrane chromatography as the efficiency of separation is highly dependent on fluid flow distribution and collection within the membrane device. We discuss a novel, laterally-fed module, designed specifically for flat-sheet membrane chromatography. The performance of the novel module was compared with that of a conventional, centrally-fed, circular membrane module. Experiments were carried out with both devices using anion-exchange membrane sheets having the same surface area and thickness, and thereby the same bed volume. Tracer experiments using either a dye or a protein (lysozyme) under non-binding condition clearly indicated superior flow distribution and collection within the novel module. This could be attributed to greater uniformity in solute flow path length. The protein binding capacities of membrane sheets of identical surface area and bed volume housed in the novel and conventional modules were compared in the breakthrough and pulse modes, using bovine serum albumin (or BSA) as the model adsorbed protein. The breakthrough experiments showed that at the same experimental conditions, the 1% breakthrough binding capacity of the membrane housed in the novel module was 5.12 times higher than that housed in the conventional module. Moreover, flow-through and elution peaks obtained with the novel membrane module were significantly sharper and more symmetrical, with lower peak width.

1. Introduction

Membrane chromatography is a relatively new purification technique which involves the use of a stack of synthetic membrane as chromatographic media [1–9]. The most attractive feature of membrane chromatography is the speed of separation. As solute transport is largely based on convection, the time taken for solute to reach its binding site during adsorption and away from it during elution is significantly lower than in column chromatography, where such transport is diffusion-limited. Membrane chromatography could therefore be faster by more than one order of magnitude, a factor which contributes towards higher productivity and decrease in product degradation by proteolysis, denaturation and aggregation. The predominance of convection also makes it easier to model membrane chromatography as the diffusion based terms in the equations could be eliminated. It is also much easier to develop thumb-rules for scaling up separation processes. Membrane chromatography is frequently scaled-up in a modular fashion, i.e. by using multiple devices either in series or in parallel. The disposable nature of membrane chromatography devices eliminates the need for equipment cleaning and revalidation is one of the main factors behind its acceptance by users in recent years.

The efficiency of membrane chromatography is critically dependent on the fluid flow distribution within the membrane device [5,8–12]. Membrane chromatography devices are commonly available in two formats: (a) stacked disks, and (b) radial flow. Both types of devices suffer from poor flow distribution which leads to shallow breakthrough and consequently poor binding capacity utilization [13–17]. Hollow fiber membrane chromatography devices are also available [7,16] but they are less commonly used. The stacked disk devices which resemble a syringe-type micro-filters are relatively easy to fabricate, and are used for preliminary process development work. However, stacked disk devices with large bed volumes are impractical and the circular shape of the membrane results in significant material wastage. Stacked disks typically have small bed heights with relatively large radial dimension (see Fig. 1). The feed enters at a location corresponding to the center of the first disk, while the flow-through is collected from the center of the last membrane in the stack. Consequently, the central region of the stack gets saturated with solute much earlier than the peripheral regions leading to poor breakthrough binding capacities. Radial flow devices have complicated design, and are used for large-scale purification. They have large dead volumes on both feed and permeate side, and a large central core for supporting the membrane, and therefore extremely poor device volume utilization [13]. The availability of devices with better design would increase the efficiency of membrane chromatography based separation processes, and this in turn could potentially make this technology more attractive to potential users. A good membrane device should give

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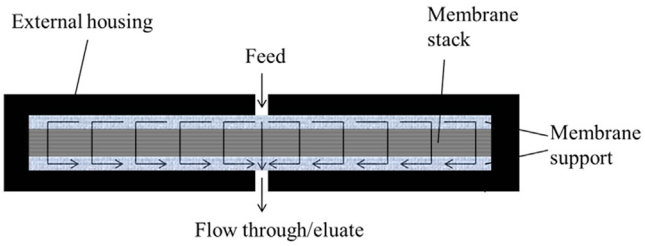

Fig. 1. Flow distribution in conventional, centrally-fed circular membrane adsorber.

a sharp solute breakthrough; have low void volume and be based on a simple design with well-defined flow path. While there is significant potential for research and development work on efficient membrane devices, mathematical modeling, operational aspects, and process optimization of membrane chromatography, relatively less has been published in the above-mentioned areas [18–23].

In this paper, we discuss a novel membrane chromatography module [24] which addresses some of the issues highlighted in the previous paragraph. The module which is shown in Fig. 2 houses a stack of rectangular flat sheet adsorptive membranes. Fluid entering the device is distributed in a lateral manner over the side of the membrane stack closer to the inlet. The fluid then enters the membrane stack at different locations along its length, flow normal to the membrane surface, and eventually emerges at the other side of the membrane stack. The fluid then flow laterally with respect to the surface of the last membrane in the stack and is collected at the device outlet. The lateral-flows on both sides of the membrane stack are parallel and in the same direction. As shown in Fig. 2, the flow path lengths are uniform which is expected to improve the efficiency of membrane utilization and thereby result in a higher breakthrough binding capacity. The performance of the novel device was compared with that of an equivalent centrally-fed, disk-based membrane module. Anion-exchange membrane sheets having the same surface area and thickness, and thereby same bed volume were used in both devices. Tracer experiments were carried out using a dye as well as a protein (lysozyme) under non-binding condition. Bovine serum albumin (or BSA) was used as model binding protein to determine the binding capacities of membrane sheets of identical surface area and bed volume housed in the novel and conventional modules were compared in the breakthrough and pulse modes. The results obtained are discussed.

2. Materials and methods

Bovine serum albumin (A2153), lysozyme (L6876), sodium phosphate monobasic (S0751), sodium phosphate dibasic (S0876), and sodium chloride (S7653) were purchased from Sigma-Aldrich (St. Louis, MO, USA). Red food dye was purchased from (McCormick, Sparks, MD, USA). Sartobind Q anion-exchange membrane sheet (94IEXQ42-001, 275 μm thickness) was purchased from Sartorius (Gottingen, Germany). Hydrophilized PVDF membrane (0.22 μm; GVWP) was purchased from Millipore (Billerica, MA, USA). All buffers and sample solutions were prepared using ultra-pure water (18.2 MΩ cm) obtained from a SIMPLICITY 185 water purification unit from Millipore (Molsheim, France).

The detailed design of the conventional circular module for housing disk-shaped membrane is shown in Fig. 3 while that of the novel module is shown in Fig. 4. The circular module had an outer diameter of 75 mm while the novel module had an external dimension of 200 mm × 40 mm. As shown in Figs. 3 and 4 membrane assemblies consisting of the adsorptive membrane sandwiched between two Teflon spacers (each of 0.508 mm thickness) was held between the top and bottom plates. The circular or rectangular spaces within the Teflon spacers on both sides of a membrane were filled with woven wire meshes which served as membrane support and liquid distributor. Appropriately positioned screws were used to hold the top and bottom plates together. The effective membrane area in both of these devices was 12.57 cm^2. The effective diameter of membrane used in the circular module which corresponded to the

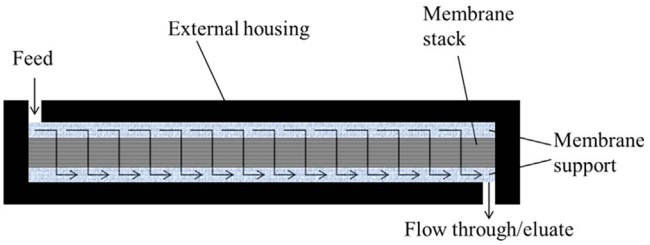

Fig. 2. Flow distribution in novel, laterally-fed, rectangular membrane adsorber.

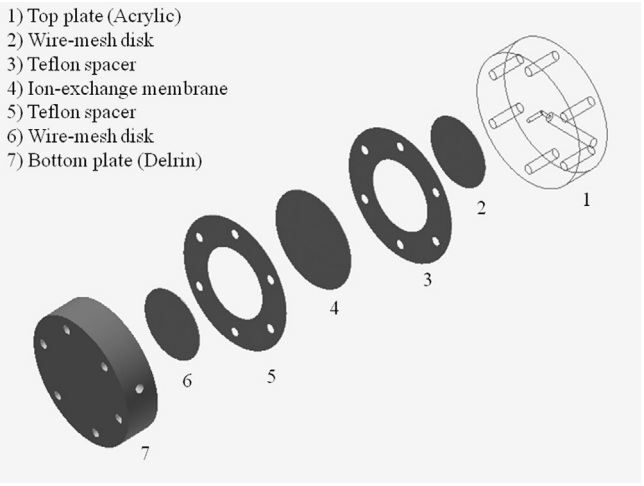

Fig. 3. Blowout diagram of conventional, centrally-fed circular membrane module (from right to left: transparent acrylic top plate, woven wire mesh support/distributor, membrane spacer, membrane disk, membrane spacer, woven wire mesh support/distributor, bottom plate).

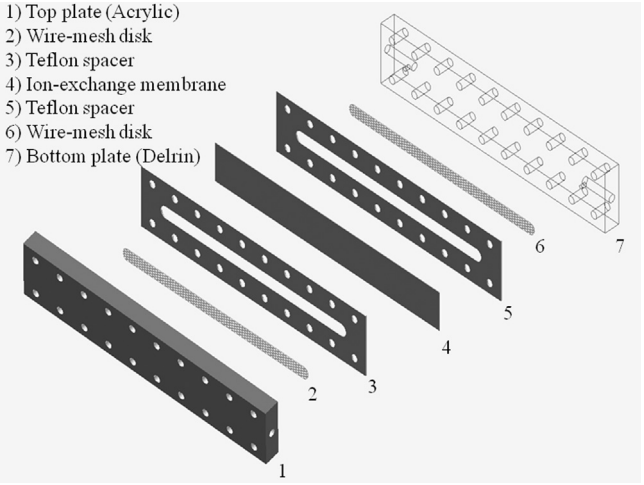

Fig. 4. Blowout diagram of novel, laterally-fed rectangular membrane module (from right to left: transparent acrylic top plate, woven wire mesh support/distributor, membrane spacer, rectangular membrane sheet, membrane spacer, woven wire mesh support/distributor, bottom plate).