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Characterization of hydrodynamics in membrane chromatography devices using magnetic resonance imaging and computational fluid dynamics

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ABSTRACT

Membrane chromatography (MC) is increasingly used in downstream processes for biomolecule purification as a large range of axial or radial flow commercial membranes is available. The design of these devices plays a major role on flow distribution and biomolecule binding. To better understand the hydrodynamic in MC devices, the velocity field was measured for the first time using magnetic resonance imaging (MRI) and calculated by computational fluid dynamics (CFD) on reconstructed geometries obtained by MRI. The CFD model solved Navier–Stokes and Brinkman equations in the free and membrane regions, respectively. Both axial flow and radial flow devices were investigated. For the axial flow device, the velocities were found higher at the periphery for all membrane bed heights. This result suggests that the whole membrane housing has an effect on flow distribution, the inlet and outlet distributors as well as the peripheral walls of the module. In the radial flow device, a high decrease in velocity was observed along the membrane bed height, which could be due to the reduction of the diameter section at the module outlet. Overall, it was concluded that MRI and CFD are powerful methods to better understand the hydrodynamics within MC devices.

1. Introduction

Membrane chromatography (MC) is an alternative technique to traditional resin chromatography. This purification method employs a microporous membrane with large pore size as the stationary phase. The major advantage of MC comes from its mass transport which is mainly convective and not limited by diffusion like in resin columns. Using MC, faster binding than in traditional columns is obtained, resulting in fast biomolecules purifications and high productivities (Ghosh, 2002; Charcosset, 2012; Boi, 2007). Furthermore, MC can be employed for single-use applications due to its simple and disposable format. This can significantly reduce capital costs of production facilities in biopharmaceutical manufacturing (Research and Markets, 2012). Nowadays, MC devices are mainly commercialized into two configurations, axial and radial flow. Axial flow devices consist of several stacked membrane discs contained in housing. The flow goes from top through the membrane bed to the outlet. Inside radial flow devices, the membrane is in the form of a spiral wound or rolled around a cylindrical core. The flow pattern is from the outside membrane cylinder to the inside core. For both MC devices, non-uniform flow distribution may limit performance by a decrease in binding capacity and poor resolution

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Nomenclature

Abbreviations

BW	acquisition bandwidth
CFD	computational fluid dynamics
CSTR	continuously stirred tank reactor
FA	flip angle
FLASH	fast low-angle shot
MC	membrane chromatography
MRI	magnetic resonance imaging
PDEs	partial differential equations
PEEK	polyetheretherketone
PFR	plug flow reactor
PIV	particle image velocimetry
RC	reinforced cellulose
RF-Pulse	resonant magnetic pulse
TE	echo time
TR	repetition time

Symbols

B_0	magnetic field
G_x	intensity of the magnetic gradient
h	membrane height
M_0	macroscopic magnetization
n	membrane length of the radial device
N	total number of data used for the calculation of the average velocities
P	pressure
r	radial coordinate
R	radius of the tube at the inlet of the MC device
T_1	characteristic time needed by the system to lose its energy and reach back the equilibrium state
T_2	time during which the vectorial sum of all the small magnetization is non-negligible
u	fluid velocity
u_{av}	average velocity at the inlet of the MC device
u_{MRI}	velocity obtained by MRI
u_{CFD}	velocity obtained by CFD
v	interstitial velocity
v_x	speed of spins traveling along the x direction
x	dimension along the x-axis
y	dimension along the y-axis
z	dimension along the z-axis
μ	dynamic viscosity
ε	membrane porosity
κ	membrane permeability
ω	pulsation of the precession
γ	magnetogyric ratio of the nucleus
γ	constant
φ_v	phase accumulated by spins
τ	duration of the magnetic gradient
ρ	density of water

(Madadkar et al., 2015). In order to improve MC performance, the understanding of the hydrodynamics within the void regions and the membrane is needed and can be obtained using mathematical modeling and non-invasive measurement (Chen et al., 2004).

Mathematical modeling of MC binding breakthrough curve can be obtained by solving transport and binding kinetic equations within the membrane region (Suen and Etzel, 1992; Shiosaki et al., 1994; Gebauer et al., 1997; Frerick et al., 2008). To match the experimental results, the real flow distribution has to be taken into account. For this purpose, a continuously stirred tank reactor (CSTR) and a plug flow reactor (PFR) in series were used to describe dead volumes and dispersion in the MC device and the experimental set-up (Boi et al., 2007; Francis et al., 2011). The velocity at the inlet of the MC module in the form of a polynomial equation was used to describe the non-symmetrical breakthrough curve shape (Schneiderman et al., 2011). Computational fluid dynamics (CFD) has been recently integrated into the MC model (Ghosh et al., 2013, 2014) to predict the velocity field in the complex geometry of the MC device. CFD can provide data which are difficult to measure experimentally, such as velocity and pressure. However, CFD may require very large computational grid for complex geometries and moderate to high Reynold numbers (Elkins and Alley, 2007), which may be computationally expensive and time consuming.

To visualize the flow distribution in the membrane devices, non-intrusive or/and quasi-non-intrusive observation methods can be used (Chen et al., 2004). The optical techniques, which employ high magnification camera or microscope to obtain real-time imaging, have been extensively studied in many applications. Particle image velocimetry (PIV) is one of the optical technique that can be applied to determine the instantaneous velocity field in applications such as ultrafiltration in a plane Plexiglass module (Gaucher et al., 2002) and cylindrical rotating filtration (Wereley et al., 2002). In the PIV system, suitable tracer particles are injected into the flow field (Chen et al., 2004). A short pulse laser system emits high power light beams to illuminate particles driven in the flow, which are digitally recorded using a high speed camera. The relative displacement of tracer particles within the flow is therefore determined. However, PIV and other optical methods are limited by instantaneous data acquisition and low resolution in the sub-micron range, as well as by the requirements for transparency and discrimination between particles. The velocity in the porous membrane thus cannot be measured. A non-optical method like MRI can improve the imaging resolution to the angstrom level. Numerous flow quantities can be measured by MRI including mean velocities, Reynolds stresses, and diffusion coefficients and tensors (Elkins and Alley, 2007).

MRI, generally used for medical diagnostics, is an imaging technique for generating spatially resolved images inside an object utilizing the interaction between an applied magnetic field and a nucleus that possesses spin (Gladden, 1994). MRI has been reported in several studies of hydrodynamic characterization within membrane modules. Pangrle et al. (1989, 1992) investigated the flow distribution in a hollow fiber membrane reactor and in a porous tube and shell module at different Reynold numbers in the laminar flow regime. The MRI technique used was a spin-echo "time of flight", which provided a 2-D image of a selected cross section based on spin-echo ^{1}H. Flow distribution in a hollow fiber bioreactor was also investigated by Hammer et al. (1990) and Heath et al. (1990). In these studies, MRI was used to measure the convective leakage flow in the extracapillary space of the hollow fiber module. The measured velocities compared well with theoretical results obtained from a solution of Poisson's equation. The authors concluded that the combination of MRI measurements and mass transfer modeling is a powerful tool for process optimization and design of membrane devices. Yao et al. (1995) mapped the flow distribution in a hollow