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A general rate model approach for the optimization of the core radius fraction for multicomponent isocratic elution in preparative nonlinear liquid chromatography using cored beads

Tingyue Gu [a],*, Mingqing Liu [a], Kwok-Shun C. Cheng [b], Senthilkumar Ramaswamy [b], Chen Wang [b]

[a] *Department of Chemical and Biomolecular Engineering, Ohio University, Athens, OH 45701, USA*
[b] *BioProcess R&D, Millipore Corporation, 80 Ashby Road, M1 North, Bedford, MA 01730, USA*

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ABSTRACT

Cored beads (also known as pellicular, superficially porous, and fused-cored beads or particles) offer advantages over fully porous beads in reduced diffusional mass transfer resistances in particle macropores and separation times in liquid chromatography (LC). They are also used to regulate bead densities. The core of a bead has a relatively small volume and yet presents a large linear distance for diffusional mass transfer inside particle macropores. Using a non-porous inert core, intraparticle diffusional mass transfer resistance can be reduced with a relatively small loss in binding capacities. In multicompnent isocratic elution chromatography, cored beads are a compromise between fully porous beads and non-porous beads. Non-porous beads completely eliminate intraparticle diffusion, providing sharp elution peaks with the shortest retention times. However, they do not provide a sufficient retention time range for peaks to separate in preparative LC because of their limited binding capacities. At the other end, fully porous beads offer the largest retention time differences, but suffering from excessive band broadening. For a particular multicomponent elution system, core radius fraction can be optimized to take the advantages of both fully porous beads and non-porous beads. This work presented a general rate model for cored beads and its numerical solution strategy. The model considered axial dispersion, interfacial mass transfer, intraparticle diffusion, and multicomponent Langmuir isotherm. Computer simulation was used to study the effects of core radius fraction on breakthrough curves and elution peaks. The model was used to optimize the core radius fraction for a preparative ternary elution system as an example case.

1. Introduction

In liquid chromatography (LC), eluites must migrate from the bulk-liquid phase to the particle phase by crossing a stagnant liquid film surrounding each particle. This is the so-called interfacial film mass transfer. Inside the particle macropores, diffusion in the stagnant liquid allows eluites to interact with the binding sites. The core section of a fully porous bead offers a disportionately small volume that corresponds to a small percentage of binding sites, but it presents a relatively large linear radial distance for diffusional mass transfer (Kirkland et al., 2000). Non-porous beads have been a success in analytical LC because they provide sharp peaks and fast separation times (Lee, 1997; Rissler, 2000; Xiang et al., 2003; Fekete et al., 2010). However, these beads do not offer sufficient binding sites for peak separations in preparative LC (Kirkland et al., 2000; Miyabe, 2008). Fully porous and non-porous beads offer two extreme cases for mass transfer and binding capacities. The former offers the largest binding capacities and diffusional intraparticle mass transfer resistance, while the latter the smallest binding capacities and complete elimination intraparticle mass transfer. In preparative- and large-scale LC, a substantial binding capacity is needed to create retention time differences among peaks. However, with fully porous beads, band broadening makes baseline separation difficult when the peaks migrate inside the column for too long. Between fully porous and non-porous beads, there is a middle ground that is better for many systems.

Cored beads (Wang et al., 2007) are a compromise between fully porous and non-porous beads. Fig. 1 is a sketch of a spherical cored bead. Cored beads are also known as pellicular (Coutinho et al., 2001; Zhou et al., 2004; Greibrokk, 2004), superficially porous (Kirkland et al., 2000), and fused-core (Manchon et al., 2010) beads or particles. Fig. 2 shows the theoretical relationships of core radius fraction with core volume fraction and shell volume

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* Corresponding author. Tel.: +1 740 593 1499; fax: +1 740 593 0873.
E-mail address: gu@ohio.edu (T. Gu).

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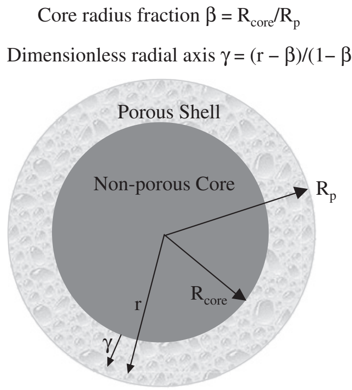

Fig. 1. Schematic of a spherical cored bead with an inert non-porous core and a porous shell.

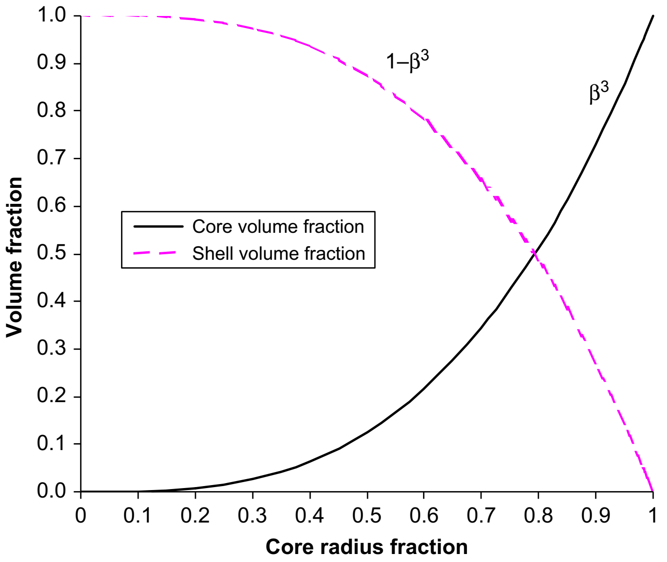

Fig. 2. Theoretical core volume and shell volume distributions as functions of core radius fraction (β).

fraction. The dashed curve in Fig. 2 indicates that the porous shell volume (including macropores) declines very slowly initially following the increase of core radius fraction before the core radius fraction reaches around 0.5.

Cored beads can be made nearly perfectly spherical with a narrow particle size distribution using suitable cores such as borosilica beads (Wang et al., 2007). This kind of spherical beads can reduce non-ideal flow inside a column. They also yield a lower column pressure drop compared to beads with smaller particle sizes (Kirkland et al., 2000; Fanigliulo et al., 2010; Pietrogrande et al., 2010). Cored beads have been used in various LC separations, especially in ion exchange (Horvath et al., 1967; Pesek and Frost, 1973; Ning et al., 1998; Wang et al., 2007). They have been used for separations of proteins and peptides (Kirkland et al. 2000; Zhou et al., 2007; Kiss et al., 2010) including proteins in proteomic research (Wang, et al., 2006), nucleotides (Horvath et al., 1967), and other compounds (Ning et al., 1998). Cabooter et al. (2010) and Fanigliulo et al. (2010) compared several commercially available fully porous and cored beads experimentally. Cored beads have also been used in gas chromatography according to Kirkland (1969).

Cored beads have a special niche in expanded bed operations because the cores allow the control of bead density through the use of cores with different densities including stainless steel cores (Palsson et al., 2000; Zhou et al., 2004). Ding and Sun (2005) fabricated gel-coated cored beads with dense magnetic cores for protein separations in a magnetically stabilized fluidized bed. The use of a rigid core relieves bed compression for soft gels (Wang et al., 2007). This means during scale-up, cored beads allow longer columns that are better for peak resolution.

Yang and Hu (1996) derived the theoretical moment expressions for elution and frontal linear chromatography with pellicular ion exchange resins. Zhou et al. (2004) used a general rate model for cored beads to obtain intraparticle diffusion coefficients. They did not provide numerical methods or simulated concentration profiles. Kaczmarski and Guiochon (2007) studied thin-shelled coated beads with a lumped particle model assuming that the concentration profile inside the thin shell could be represented by a single averaged concentration value. To compare with fully porous beads that can have steep concentration changes, they used a standard general rate model for the fully porous beads. More recently, Li et al. (2010) performed optimization of core size for linear chromatography by minimizing height equivalent theoretical plate (HETP) number.

So far, in the open literature, there is no theoretical comparison of fully porous beads, cored beads, and non-porous beads in a systematic way to illustrate the principle of optimization of the core radius fraction for designing cored beads used in nonlinear preparative multicomponent isocratic elution. This work presented a general rate model for cored beads, which considered axial dispersion, interfacial film mass transfer, intraparticle diffusion, and multicomponent Langmuir isotherm. A theoretical three-component elution case study was carried out using the model to demonstrate the existence of an optimal core radius fraction for faster baseline separation.

2. Model and numerical methods

The following model equations describe mass transfer in the column bulk-fluid phase and in the stationary liquid phase inside particle macropores. Cored beads are assumed to have a uniform particle size (R_p) and core size (R_{core}). The inner core cannot be penetrated and there is only diffusion (no convection) in the porous shell. The column is assumed to be isothermal:

$$-D_{bi}\frac{\partial^2 C_{bi}}{\partial Z^2}+v\frac{\partial C_{bi}}{\partial Z}+\frac{\partial C_{bi}}{\partial t}+\frac{3k_i(1-\varepsilon_b)}{\varepsilon_b R_p}(C_{bi}-C_{pi,R=Rp})=0 \tag{1}$$

$$(1-\varepsilon_p)\frac{\partial C^*_{pi}}{\partial t}+\varepsilon_p\frac{\partial C_{pi}}{\partial t}-\varepsilon_p D_{pi}\frac{1}{R^2}\frac{\partial}{\partial R}\left(R^2\frac{\partial C_{pi}}{\partial R}\right)=0 \tag{2}$$

Multicomponent Langmuir isotherm can be expressed as

$$C^*_{pi}=\frac{a_i C_{pi}}{1+\sum_{j=1}^{N_s} b_j C_{pj}} \tag{3}$$

To reduce the number of variables, the PDE system is non-dimensionalized using the following dimensionless variables and parameters:

$$c_{bi}=C_{bi}/C_{0i}, c_{pi}=C_{pi}/C_{0i}, c^*_{pi}=C^*_{pi}/C_{0i}, r=R/R_p,$$
$$z=Z/L, Pe_{Li}=vL/D_{bi}, Bi_i=k_iR_p/(\varepsilon_p D_{pi}), \eta_i=\varepsilon_p D_{pi}L/(R_p^2 v),$$
$$\xi_i=3Bi_i\eta_i(1-\varepsilon_b)/\varepsilon_b, \tau=vt/L$$

Eqs. (1)–(3) can be transformed into dimensionless forms as follows:

$$-\frac{1}{Pe_{Li}}\frac{\partial^2 c_{bi}}{\partial z^2}+\frac{\partial c_{bi}}{\partial z}+\frac{\partial c_{bi}}{\partial \tau}+\xi_i(c_{bi}-c_{pi,r=1})=0 \tag{4}$$

$$(1-\varepsilon_p)\frac{\partial}{\partial \tau}c^*_{pi}+\varepsilon_p\frac{\partial c_{pi}}{\partial \tau}-\eta_i\frac{1}{r^2}\frac{\partial}{\partial r}\left(r^2\frac{\partial c_{pi}}{\partial r}\right)=0 \tag{5}$$