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Achieving quasi-adiabatic thermal environment to maximize resolution power in very high-pressure liquid chromatography: Theory, models, and experiments

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ABSTRACT

A cylindrical vacuum chamber (inner diameter 5 cm) housing a narrow-bore 2.1 mm × 100 mm column packed with 1.8 μm HSS-T_3 fully porous particles was built in order to isolate thermally the chromatographic column from the external air environment. Consistent with statistical physics and the mean free path of air molecules, the experimental results show that natural air convection and conduction are fully eliminated for housing air pressures smaller than 10^{-4} Torr. Heat radiation is minimized by wrapping up the column with low-emissivity aluminum-tape (emissivity coefficient $\epsilon = 0.03$ vs. 0.28 for polished stainless steel 316). Overall, the heat flux at the column wall is reduced by 96% with respect to standard still-air ovens. From a practical viewpoint, the efficiency of the column run at a flow rate of 0.6 mL/min at a constant 13,000 psi pressure drop (the viscous heat power is around 9 W/m) is improved by up to 35% irrespective of the analyte retention. Models of heat and mass transfer reveal that (1) the amplitude of the radial temperature gradient is significantly reduced from 0.30 to 0.01 K and (2) the observed improvement in resolution power stems from a more uniform distribution of the flow velocity across the column diameter. The eddy dispersion term in the van Deemter equation is reduced by 0.8 ± 0.1 reduced plate height unit, a significant gain in column performance.

1. Introduction

Answering the need for separating more and more complex sample mixtures, very high-pressure liquid chromatography (vHPLC) emerged in the mid-2000s with the successful preparation of high-strength sub-2 μm fully porous particles in combination with high-pressure pumps operating up to 1 kbar [1–3]. 10 cm long narrow-bore columns packed with such fine particles can intrinsically provide up to 30,000 plates, e.g., the same resolution power as that of a 30 cm long column packed with 5 μm particles but run at a 10 times faster linear velocity [4].

The effects of high pressure in liquid chromatography have been anticipated from a physico-chemical viewpoint [5]. Among the numerous effects of pressure on chromatographic properties, and despite the reduction of the column inner diameter from 4.6 to 2.1 mm, viscous heat is not negligible in vHPLC: as a result, the temperature of the column is no longer uniform and stationary radial and axial temperature gradients are formed [6,7]. These cause reproducibility issues regarding retention and efficiency data if the analyst is not meticulous enough in controlling the nature of the thermal environment surrounding the column [8].

While both temperature and pressure longitudinal gradients are not detrimental for vHPLC performance [9], radial temperature gradients are [8,10–12]. Two independent mechanisms affect column efficiency simultaneously: (1) since retention is temperature-dependent (at least for retained compounds), sample molecules in the hot center of the bed move faster than those present in the cooler wall region. (2) Eluent viscosity is both pressure and temperature dependent, so, the flow profile is inevitably dependent on the imposed pressure and temperature gradients across and along the column. The minimization of transverse temperature gradients has motivated research investigations using intermediate eluent cooling [13] or using a more adiabatic oven by wrapping the column inside isolating foams [8,14]. Yet, these strategies did not improve markedly the efficiency of columns placed in standard still-air oven.

New approaches are then needed in order to fully isolate the chromatographic column from the external thermal environment. Heat transfer at the column wall is controlled by natural air convection, air conduction, and electromagnetic radiation [15]. In this work, we suggest placing the column inside a vacuum housing, in

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which the air pressure is progressively reduced from 1 atm down to 10^{-5} Torr, to completely eliminate air convection and conduction. A 2.1 mm × 100 mm column packed with sub-2 μm fully porous particles is run at a maximum pressure close to 13,000 psi in order to produce a large amount of viscous heat (around 9 W/m). Additionally, we propose to wrap up the column with a low-emissivity material to minimize heat losses by radiation. The effects of vacuum air pressure, flow rate, and of the emissivity coefficient of the surface wall on the column efficiency is modeled, measured, and discussed in details.

2. Theory

2.1. General definitions and relationships

A list of physico-chemical parameters, their symbol, the intensity they take in this work, and the fundamental relationships between them, are given. The next two sections cover the basics of column efficiency in liquid chromatography and of heat transfer due to conduction, natural convection, and thermal radiation.

2.1.1. Chromatography and column efficiency

The dimensions of the chromatographic column are r_c = 1.05 mm (inner radius), L = 10 cm (length), and r_e = 3.00 mm (outer radius of the stainless steel tube). It is packed with HSS-T_3 fully porous particles. The average particle diameter is d_p = 1.8 μm. The internal, total, and external porosities of this column are ϵ_p = 0.44 (measured from helium pycnometry/nitrogen sorption), ϵ_t = 0.65 (measured from the elution volume of toluene in pure acetonitrile), and ϵ_e = 0.38 (determined from the measurement of ϵ_p and ϵ_t), respectively. Accordingly,

$$\epsilon_e = \frac{\epsilon_t - \epsilon_p}{1 - \epsilon_p} \tag{1}$$

The column efficiency, $N = (L/hd_p)$, is only defined under isothermal conditions. h is the reduced plate height given by:

$$h = \frac{B}{\nu} + \frac{\omega_1 \nu}{1 + (\omega_1/2\lambda_1)\nu} + \frac{\omega_2 \nu}{1 + (\omega_2/2\lambda_2)\nu} + \frac{\omega_t \nu}{1 + (\omega_t/2\lambda_t)\nu} + C\nu \tag{2}$$

where ν is the reduced interstitial linear velocity defined by

$$\nu = \frac{u d_p}{D_m} \tag{3}$$

where D_m is the bulk diffusion coefficient and u is the interstitial linear velocity given by

$$u = \frac{F_v}{\epsilon_e \pi r_c^2} \tag{4}$$

where F_v is the applied flow rate.

In Eq. (2), B is the reduced longitudinal diffusion coefficient, C is the reduced solid–liquid mass transfer resistance coefficient due to the finite diffusivity of the sample across the porous particle, ω_1 and ω_2 are coefficients related to eddy dispersion controlled by a molecular diffusion exchange for trans-channel (subscript 1) and short-range inter-channel (subscript 2) eddies, λ_1 and λ_2 are the corresponding coefficients related to eddy dispersion controlled by a convection exchange, and ω_t and λ_t are the same coefficients related to long-range eddies [16–19]. For well-packed columns with fully porous particles and an external porosity ϵ_e = 0.38, ω_1 = 0.003, λ_1 = 0.375, ω_2 = 0.11, λ_2 = 0.18 [17]. The coefficients ω_t = 0.22 and λ_t = 1.13 were best estimated from the h vs. ν plot of n-hexanophenone ($D_m = 1.16 \times 10^{-5}$ cm^2/s) at 303 K for a mixture of acetonitrile and water (50/50, v/v) as the eluent and for the 2.1 mm × 100 mm column packed with 1.8 μm HSS-T_3 particles. For instance, under quasi-adiabatic conditions and for n-hexanophenone (k' = 13.4), the best estimated values of the coefficients B and C were 12.8 and 0.0058, respectively. Note that the contribution of a slow adsorption–desorption process of the analyte on the reduced plate height in Eq. (2) was neglected for small molecules [20].

2.1.2. Heat transfer

2.1.2.1. Conduction. The thermal conductivities of bulk silica, C_{18} octadecyl chains, water, and acetonitrile are $\lambda_{SiO_2} = 1.40$ W/m K, $\lambda_{C_{18}} = 0.36$ W/m K, $\lambda_{H_2O} = 0.60$ W/m K, and $\lambda_{ACN} = 0.19$ W/m K, respectively [6]. The volume fractions of bulk silica and C_{18}-bonded chains in HSS-T_3 particles are $\phi_{SiO_2} = 0.71$ and $\phi_{C_{18}} = 0.29$. The volume fractions of water and acetonitrile in the interstitial eluent are $\phi_{e,H_2O} = \phi_{e,ACN} = 0.5$. The volume fractions of water and acetonitrile in the internal eluent inside the 100 Å mesopores of the HSS-T_3 particles are $\phi_{p,H_2O} = 0.25$ and $\phi_{p,ACN} = 0.75$ due to the preferential adsorption of acetonitrile onto silica–C_{18} surface [21]. The effective thermal conductivity, $\lambda_{eff,ij}$, of a heterogeneous material made of two homogeneous materials i and j randomly distributed in space is estimated from [22]:

$$\lambda_{eff,ij} = \phi_i^2 \lambda_i + \phi_j^2 \lambda_j + 4\phi_i\phi_j \frac{\lambda_i \lambda_j}{\lambda_i + \lambda_j} \tag{5}$$

Eq. (5) is used to estimate the effective thermal conductivity (0.460 W/m K) of a packed bed (HSS-T_3 fully porous particles) immersed in the mobile phase (acetonitrile/water eluent mixture, 50/50, v/v).

The thermal conductivity of air at atmospheric pressure is $\lambda_{air}(P^0) = 0.026$ W/m K. The effect of pressure, P (Pa), on the thermal conductivity of air between two planes separated by a distance d is given by [23]:

$$\lambda_{air}(P, T) = \frac{\lambda_{air}(P^0)}{1 + c(T/Pd)} \tag{6}$$

where T is the temperature and c is a constant equal to 7.6×10^{-5} N/m K for a thermal accommodation coefficient of α_c = 1. The thermal accommodation coefficient is an empirical parameter that measures momentum and heat transfer to surfaces. It depends on the unknown nature of the gas–surface interaction mechanism and is written

$$\alpha_c = \frac{E_{in} - E_r}{E_{in} - E_w} \tag{7}$$

where E_{in} is the incident energy flux, E_r is the reflected energy flux, and E_w is the energy flux that would be achieved if the reflected molecules were emitted in thermal equilibrium at the surface temperature. The thermal accommodation coefficient varies between unity (complete accommodation, diffuse reflection, $E_r = E_w$) and zero (adiabatic, specular reflection, $E_r = E_{in}$). For instance, α_c = 0.8 for nitrogen/machined and highly-polished stainless steel surfaces [24].

Accordingly, a more general expression for $\lambda_{air}(P, T)$ was derived [25]:

$$\lambda_{air}(P, T) = \frac{\lambda_{air}(P^0)}{1 + 2(2\gamma/(\gamma + 1))(1/Pr)((2 - \alpha_c)/\alpha_c)(l(P)/d)} \tag{8}$$

where γ is the ratio of specific heat (γ = 1.4 for air), Pr is the Prandtl number (Pr = 0.7 for air), and $l(P)$ is the mean free path in free space (the average travel distance between two consecutive collisions) of air molecules. The dependence of $l(P)$ as a function of pressure is derived from the ideal gas kinetic theory [26]:

$$l(P) = \frac{k_B T}{\sqrt{2}\pi P r^2} \tag{9}$$