The effects of chain length, embedded polar groups, pressure, and pore shape on structure and retention in reversed-phase liquid chromatography: Molecular-level insights from Monte Carlo simulations

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ABSTRACT

Particle-based simulations using the configurational-bias and Gibbs ensemble Monte Carlo techniques are carried out to probe the effects of various chromatographic parameters on bonded-phase chain conformation, solvent penetration, and retention in reversed-phase liquid chromatography (RPLC). Specifically, we investigate the effects due to the length of the bonded-phase chains (C_{18}, C_8, and C_1), the inclusion of embedded polar groups (amide and ether) near the base of the bonded-phase chains, the column pressure (1, 400, and 1000 atm), and the pore shape (planar slit pore versus cylindrical pore with a 60 Å diameter). These simulations utilize a bonded-phase coverage of 2.9 μmol/m^2 and a mobile phase containing methanol at a molfraction of 33% (about 50% by volume). The simulations show that chain length, embedded polar groups, and pore shape significantly alter structural and retentive properties of the model RPLC system, whereas the column pressure has a relatively small effect. The simulation results are extensively compared to retention measurements. A molecular view of the RPLC retention mechanism emerges that is more complex than can be inferred from thermodynamic measurements.

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1. Introduction

In high performance liquid chromatography (HPLC), the majority of separations are carried out with stationary phases containing chemically-bonded alkyl chains and mobile phases containing mixtures of water and organic modifiers, a mode referred to as reversed-phase liquid chromatography (RPLC) [1–3]. Many aspects of the retention mechanism(s) of RPLC are elusive [4–7] and require a multifaceted approach towards understanding a separation process which may appear to be naively simple. However, the basic question of whether solutes are retained by a partitioning or an adsorption mechanism has only recently been probed at the atomic level using particle-based Monte Carlo simulations and the answer is more complicated than either a simple adsorption or partition mechanism would account for [8]. This is only one of many questions concerning the inner-workings of the RPLC method that we believe molecular simulation techniques can answer.

Part of the difficulty in studying the mechanism of RPLC lies in preparing well-controlled model bonded phases from a synthetic

point of view [9]. The support materials and conditions of chemical bonding must be extremely well understood and characterized to elicit a mechanistic detail from retention measurements. Although great strides have been made in using spectroscopic techniques for probing the bonded chain conformation and the solvent environment [10–13], spectroscopic techniques usually involve averaging over time and space. Hence, they offer little insight into the conformation of individual grafted chains, the penetration of solvent into various regions of the stationary phase, and the spatial and orientational preferences of solute molecules within and near the stationary phase. It is these questions and more that continue to drive research into the most fundamental aspects of RPLC.

Following up on earlier work by Klatte and Beck [15] and Slusher and Mountain [14] who investigated the transfer of a methane solute in model RPLC systems, we have recently examined the chain conformation, solvent penetration, and retention thermodynamics [8,16–21] of various RPLC systems via particle-based simulations using efficient sampling algorithms and accurate force fields. The previous studies investigated the effects of mobile-phase composition for water–methanol [8,16,17] and water–acetonitrile mixtures [21], the grafting density of dimethyl octadecylsilane bonded phases [19,20], and the inclusion of embedded ether and amide functionalities in the bonded-phase ligands [18]. These previous studies utilized bonded-phase chains with a backbone consisting

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of 18 carbon, nitrogen, or oxygen atoms grafted onto a planar slit pore with exposed (1 1 1) surfaces of a slab of β-cristobalite [22] and at a column pressure of 1 atm. In the current study, we explore additional chromatographic parameters that include the materials parameters of length of the alkyl chains and shape of the pores carved from β-cristobalite, and the instrumental parameter of (average) column pressure. Since reduction of the chain length leads to an increase of the polarity of the retentive phase, we also include a comparison to chains with embedded polar groups (EPG).

2. Simulation methodology

The workhorse of this simulation study is the coupled–decoupled configurational-bias Monte Carlo (CBMC) method [23–26] applied in the isobaric-isothermal version of the Gibbs ensemble [27,28]. The simulations make use of three periodic simulation boxes that are in thermodynamic contact but do not share an explicit interface (see Fig. 1). The first of these boxes contains the stationary phase. This stationary phase is either represented by a slit pore with a planar silica surface or by a cylindrical pore with a curved silica surface. The second and third boxes contain a mobile-phase reservoir and a helium vapor phase.

In this research all simulations are carried out with a 33% mol-fraction methanol mobile phase (about 50% by volume) and at a temperature of 323 K. The planar slit pore setup is used for our studies of chain length dependence (by using C_{18}, C_8, or C_1 chains), the properties of polar embedded phases (alkyl, ether, or amide phases) and pressure effects (1, 400, or 1000 atm). The cylindrical pore simulations utilize C_{18} chains and a pressure 400 atm in order to compare to the corresponding slit pore simulation. The higher pressure of 400 atm is used for this simulation, rather than 1 atm, to avoid any possible issues with dewetting of the small pore at lower pressures [29,30].

The simulation box for the planar slit pore setup is elongated in the z-direction with $L_x = 20.0$, $L_y = 26.0$, $L_z = 90.0$ Å. In the center of this box is a five layer slab of β-cristobalite (≈ 20 Å thick) with its two (1 1 1) surfaces exposed. Stationary-phase chains are grafted to the surface silanol sites on this surface at a coverage of 2.9 μmol/m^2, resulting in a residual (all vicinal) silanol density of 4.8 μmol/m^2. The initial arrangement of chains is generated by randomly choosing silanol sites, but avoiding close chain contacts [22]. For our studies of chain length, we simply use either trimethyl, dimethyl octyl, or dimethyl octadecyl silane ligands. The polar embedded phases are generated by inserting an EPG three methylene segments up from the silicon link atom, i.e., $-$Si(CH$_3$)$_2-$(CH$_2$)$_3-$EPG$-$(CH$_2$)$_x-$CH$_3$. For the ether phase the EPG is $-$O$-$CH$_2-$CH$_2-$O$-$ and for the amide phase it is $-$NH$-$CO$-$. The value of x is chosen in a manner that the total number of backbone segments is the same as the C_{18} alkyl phase, i.e., $x = 10$ for the ether phase and $x = 12$ for the amide phase. It should be noted that for each chain, both polar phases possess four hydrogen bonding sites: 4 acceptor sites for the ether phase and 1 donor and 3 acceptor sites for the amide phase. In the planar slit pore setup, there are two surfaces of the silica slab (separated by about 70 Å) and each surface has a different random arrangement of grafting points, but these same grafting points are used throughout this study regardless of chain length, chain chemistry, or system pressure.

The cylindrical pore is setup by first generating a slab of β-cristobalite with $L_x = 71.7$, $L_y = 21.5$, and $L_z = 71.7$ Å. A cylinder of diameter 60 Å is cut out of this slab by removing all atoms within 30 Å of the center of the slab's x–z plane. The resulting under-coordinated silicon and oxygen atoms at the cylinder's surface are capped with hydroxyl groups and hydrogen atoms, respectively. These new silanol sites are then randomly chosen as grafting sites for the alkyl chains (again, avoiding chain overlap) until a surface coverage of about 2.9 μmol/m^2 is achieved. The resulting density
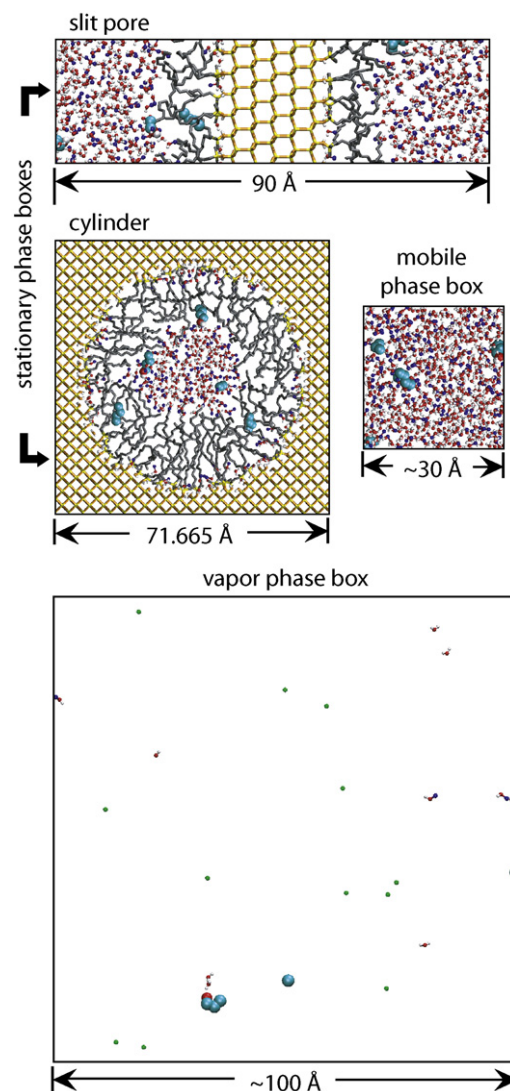
Fig. 1. Setup for the Gibbs ensemble simulations. The simulations make use of three separate simulation boxes, a box containing the stationary phase with either a planar slit or a cylindrical pore shape (top and middle left, respectively), a bulk mobile-phase box (middle right), and a vapor-phase box (bottom). In this diagram, water and methanol molecules are shown in the ball and stick representation with methyl groups, oxygens, and hydrogens in red, white, and blue, respectively. The stationary phase is depicted as tubes with CH$_x$ groups in gray, silicon in yellow, oxygen in orange, and hydrogen in white. Solute molecules are represented by larger spheres with CH$_x$ groups in cyan, oxygen in red, and hydrogen in white. Helium atoms in the vapor phase are shown as smaller green spheres.

of residual silanol groups is 5.8 μmol/m^2. However, roughly a third of these are geminal and the total density of hydroxyl groups at the silica surface is 7.8 μmol/m^2, i.e., 60% higher than for the slit pore setup.

The second and third simulation boxes contain a mobile-phase reservoir and a helium vapor phase. These boxes are cubic and their volumes are allowed to adjust in response to the external (column) pressure, whereas the silica substrate is viewed as incompressible and, hence, the box dimensions of the stationary-phase box are not allowed to change. Solvent and solute molecules are allowed to transfer between the three boxes with particle interchange [25,31] and identity exchange moves [32,33]. These moves ensure that the chemical potentials of each of the species is the same in all three boxes. Thus, the presence of the mobile-phase reservoir ensures that the chemical potentials of the water and methanol molecules in the stationary-phase box are exactly the same as in the