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A new view on surface diffusion from molecular dynamics simulations of solute mobility at chromatographic interfaces

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ABSTRACT

The behavior of solutes at the interface formed between a stationary surface and a bulk liquid lies at the heart of liquid chromatography. The diffusion coefficient of a solute in the interfacial region is an important component of the solute's mass transfer through the chromatographic bed, but a detailed understanding of solute diffusion at chromatographic interfaces, particularly of solutes in an adsorbed state, has not been reached so far. We investigate this issue through molecular dynamics simulations of two solutes (*n*-butane and 1-propanol) at two complementary interfaces that represent conditions in reversed-phase and hydrophilic interaction liquid chromatography (RPLC and HILIC, respectively). The RPLC model consists of a planar silica surface covered with a hydrophobic bonded phase (C_{18} chains) and a 90/10 (v/v) water–acetonitrile mixture; the HILIC model consists of a planar silica surface bearing isolated, single silanol groups and a 10/90 (v/v) water–acetonitrile mixture. Our data show that the solute diffusion coefficient is linked to the local solvent composition and the structural organization in the interfacial region. In the HILIC system, the solute diffusion coefficient decreases continuously over the interfacial region, ending in a quasi-frozen state at the hydrophilic silica surface. In the RPLC system, the solute diffusion coefficient goes through a maximum in the interface region, where the C_{18} chains meet the liquid mobile phase, before decreasing towards the silica surface. Our results explain the experimentally observed phenomenon of surface diffusion in RPLC by the presence of an ACN ditch between bonded phase and W-rich mobile phase, in contrast to the structured W-rich layer at a bare-silica surface in HILIC which prohibits surface diffusion.

1. Introduction

The development of liquid chromatography as one of the most important separation techniques has proceeded mainly along two lines: empirical knowledge gathered from the extensive collection of experimental (chromatographic and spectroscopic) data and technical innovations in particle technology, column packing, and equipment design [1–6]. A detailed, molecular-level understanding of the mechanism(s) by which solutes dissolved in the (liquid) mobile phase are retained on the (solid) stationary phase, however, was still lacking at a time when liquid chromatography was already a technically well developed and widely applied separation method. Since then, molecular simulation methods have enabled the visualization and quantification of the processes involved in solute retention in liquid chromatography and contributed much to the understanding of the chromatographic interface as a special form of solid–liquid interface.

The majority of molecular simulation studies of chromatographic interfaces focused on reversed-phase liquid chromatography (RPLC) [7], which has been considered as the most important (i.e., the most widely applied) liquid chromatography method over the past decades. In RPLC, the stationary phase takes the form of alkyl chains (typically C_8, C_{18}, C_{30}, with C_{18} being the most popular choice) that are chemically bonded to the solid silica support [8]. The chemical modification does not reach every silanol group on the silica surface. A fraction of these unreacted (residual) silanol groups can be modified with a short alkyl ligand, a process called endcapping. For steric reasons, however, surface coverage with alkyl ligands is never complete, so that some residual silanol groups remain on the silica support [9]. The mobile phase in RPLC is typically a mixture of water (W) and methanol or W and acetonitrile (ACN). In either case, the stationary phase is more

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hydrophobic than the mobile phase in RPLC. The formal complement to RPLC is hydrophilic interaction liquid chromatography (HILIC), a method that gained widespread acceptance only during the last decade [10–12]. In HILIC, the stationary phase is more hydrophilic than the mobile phase. HILIC offers a wider variety of stationary phase chemistries than RPLC – from bare (unmodified) silica to bonded phases with polar end groups that may or may not be charged – but the mobile phase is generally a W–ACN mixture with high ACN content.

The characteristics of the chromatographic interface have been elucidated from a series of molecular simulation studies for RPLC [13–28] and HILIC [29–34]. The most thorough characterization of the RPLC interface has come from Siepmann and co-workers [7]. According to solvent density profiles received from Monte Carlo simulations of a planar silica surface modified with C_{18} chains at a grafting density of 2.9 μmol/m^2 and an aqueous–organic mobile phase [16,24], the RPLC system contains three regions: (i) the bonded-phase region (C_{18} chains), where the total solvent density is depleted; (ii) the interface region, where the ends of the C_{18} chains meet the liquid mobile phase and the total solvent density increases from 10% to 90% of its bulk value; (iii) the bulk liquid region, where the solvent density of each species reflects the mobile phase composition. In the interface region, the density of the organic solvent (methanol or ACN) is enriched (and the W density depleted) compared with the bulk liquid. This enrichment increases when the mobile phase contains a high W fraction [24] and when the grafting density of the C_{18} chains (the surface coverage) is increased [18]. The characterization of a comparable HILIC interface comes from molecular dynamics (MD) simulations of a planar, unmodified silica surface and a W–ACN mobile phase [33,34]. The hydrophilic unmodified silica surface attracts and accumulates W molecules from the mobile phase, leading to the formation of a W-rich layer at the surface. The W-rich layer consists of a rigid and diffuse part, which are distinguished by the influence the silica surface has on their properties. The properties of the rigid part are governed by the silica surface, the properties of the diffuse part are influenced by silica surface and mobile phase alike. As for the RPLC system, three regions can be distinguished: (i) the rigid W layer, consisting mostly of W molecules that are tightly hydrogen-bonded to the silica surface; (ii) the diffuse W layer, over which the W density decreases from the high values of the rigid W layer towards bulk liquid values; and (iii) the bulk liquid region. Though not covalently bound, the rigid W layer is nearly as permanently attached to the silica surface as the bonded phase in RPLC. Thus, the diffuse W layer is the interface between functional stationary phase (silica surface plus adsorbed rigid W layer) and the bulk mobile phase.

In a typical liquid chromatography column [8,9], which is a stainless-steel cylinder densely packed with mesoporous silica particles (whose surface has or has not been chemically modified), the chromatographic interface is located inside the mesoporous particles. When the mobile phase is pumped through the column, solutes move by pressure-driven flow between the silica particles, but traverse the mesoporous particles by diffusion. Intraparticle diffusion is thought to consist of pore diffusion and surface diffusion [35,36]. Pore diffusion refers to solute migration in the pore liquid (the stagnant mobile phase) and is described by reducing the solute diffusion coefficient in the bulk mobile phase by an obstruction factor that accounts for the confined and possibly tortuous pore space. Surface diffusion describes the migration of solutes in an adsorbed state. Surface diffusion is an important contribution to the overall mass transfer in porous adsorbent systems where solutes encounter solid–gas or solid–liquid interfaces and the mechanism(s) by which surface diffusion operates is much discussed [37–43]. In general, surface diffusion is offered as an explanation for unusually high intraparticle mass transfer rates in porous adsorbents. In RPLC specifically, surface diffusion is held responsible when solute intraparticle diffusivities larger than the solute's molecular diffusion coefficient in the bulk mobile phase are observed [5,40,42,44,45]. Interestingly, the

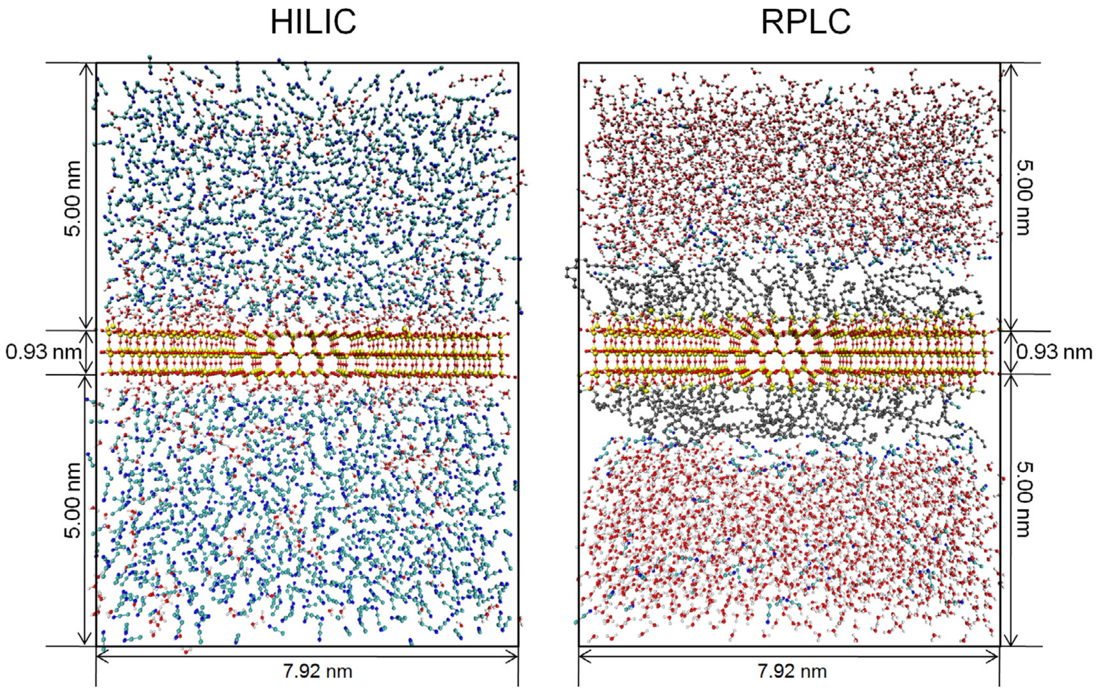

Fig. 1. Snapshots visualizing the two investigated systems. HILIC system: planar silica surface covered with single silanol groups and equilibrated with a 10/90 (v/v) W/ACN mobile phase. RPLC system: the same silica surface modified with alkyl chains (C_{18} chains and endcapping groups) and equilibrated with a 90/10 (v/v) W/ACN mobile phase. Atoms and united-atom groups are color-coded as follows: Si: yellow, O: red, H: white, N: blue, C/CH_3 (ACN): cyan, CH_2/CH_3 (alkyl chains): gray. (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article.)