Critical Conditions of Adhesion and Separation of Functionalized Nanoparticles on Polymer Grafted Substrates

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ABSTRACT: Emerging technologies of production and processing of functionalized nanoparticles (NP) require advanced methods of NP characterization and separation. While various methods are available for NP separation by size, there are no efficient methods for NP separation by surface chemistry. Using extensive dissipative particle dynamics simulations, this work investigates the mechanisms of NP adhesion and flow in polymer brush (PB)-grafted pore channels searching for the conditions for size-independent separation of NPs that are similar to the critical conditions of liquid chromatography of polymers. We consider interactions of NPs functionalized by hydrophilic and hydrophobic ligands with PBs, in which conformation and adhesion properties are controlled by the solvent quality varied with the composition of thermodynamically good and poor solvent components. The NP-PB adhesion is characterized by the free energy landscape calculated by the ghost tweezers simulation method that mimics the experimental technique of optical tweezers. The NP Henry constant and the respective partition coefficient are calculated depending on the NP size and ligand composition at varying solvent quality. Our findings demonstrate that, with the decrease of solvent quality, the NP elution undergoes a transition from the size-exclusion mode with larger NPs having shorter retention time to the adsorption mode with the reverse order of elution. This transition, which occurs in a narrow range of solvent composition, signifies the so-called “critical” point of adsorption that strongly depends on the NP functionalization. The dynamics of NP axial dispersion in the isocratic and gradient elution modes is characterized employing a convective-diffusion model. We show that the NPs can be effectively separated by surface chemistry at the critical points of adsorption, using the gradient mode of interaction NP chromatography with controlled variation of the solvent composition.

1. INTRODUCTION

Nanoparticles (NPs) find numerous applications in biosensing,12 imaging,3 supercapacitors,4 light-emitting diodes (LEDs),56 solar cells,78 and nanoelectronic devices.9 NPs functionalized with specific molecules are used in diagnostics and therapeutics,10,11 as drug carriers, and nanoporous biomaterials.12 Engineering and functional properties of NPs are sensitive to their size, shape, and surface chemistry, and advanced methods of NP characterization and separation are required for the quality control during NP production and processing. While various methods are available for NP separation by size and shape,13,15 there are no efficient methods for NP separation by surface properties, such as the degree of hydrophobicity and surface heterogeneity, that are especially important in case of NPs modified by specific functional molecules or ligands.21,23 It is highly desirable to develop techniques for NP chromatography based on the specifics of NP interactions with the stationary phase, reminiscent to the established techniques of interaction polymer chromatography.24,26 Most beneficial would be a method capable of size-independent separation of NPs by surface chemistry similar to the method of liquid chromatography at critical conditions (LCCC) for molecular-weight-independent separation of polymers by their composition and microstructure.27–32

The first advance in this direction was made in our recent work,33 which explored the conditions of chromatographic separation of NPs on porous substrates grafted with polymer brushes in a binary mixture of thermodynamically “good” and “poor” solvents, using dissipative particle dynamics (DPD) simulations. In this system, the PB played a role of a stationary phase to which NP may adhere and be retained. We showed that the NP adhesion is dependent on the PB conformation and the different separation modes
with the transition from the size exclusion mode with larger particles having shorter retention time, which is characteristic to conventional separation techniques of size exclusion chromatography (SEC)\textsuperscript{17} and hydrodynamic chromatography (HDC),\textsuperscript{18} to the adsorption mode with the reverse sequence of elution. In the present paper, we consider separation of NPs functionalized by different types of ligands and show that the crossover between the size exclusion and adsorption modes occurs for NPs of given surface chemistry in a narrow range of solvent compositions with approximately size-independent elution, similar to the critical conditions of adsorption observed in polymer separation by LC. These findings lay out a foundation for the interaction NP chromatography at critical conditions (INPCC) and inform the design of chromatographic columns and solvent selection for efficient separation of NPs by surface chemistry.

The specifics of NP-PB interactions play the central role in the process of NP separation on polymer grafted substrates, as well as in various applications of NP-PB systems such as PBs doped by NPs used in sensors and biomedical devices,\textsuperscript{34} fabrication of nanocomposites,\textsuperscript{35,36} lubrication,\textsuperscript{37} stabilization of colloids,\textsuperscript{38,39} and manipulation of nanoobjects on surfaces.\textsuperscript{40} Utilization of PB-grafted substrates in NP separation in the SEC has been investigated recently.\textsuperscript{41} NP adhesion to PBs can be controlled by varying the solvent composition\textsuperscript{42,43} that affects the PB conformation. Upon worsening of solvent quality and respective PB contraction, the free energy of NP-PB adhesion generally decreases and entropic repulsion due to NP immersion into PB. The entropic effects dominate when PB is expanded in good solvent, while the enthalpic effects dominate when PB is collapsed in bad solvent. As shown in ref 33, the NP elution in a PB-grafted channel undergoes a transition from the completely repulsive size exclusion mode in the good solvent to an adsorption mode upon addition of the poor solvent component. This observation suggested a possibility of existence of so-called critical point of adsorption (CPA),\textsuperscript{24} at which the entropic and enthalpic effects are compensated and the NP elution is size-independent as in the LC. In this work, we confirm this hypothesis and show that the CPA of functionalized NP to PB in binary solvent can be defined as a particular solvent composition, which corresponds to the transition between the size exclusion and adsorption modes and is dependent on the NP surface chemistry. Note that in contrast to polymer adsorption, the introduced CPA of NP adhesion to PB is not related to any critical phenomenon, but it rather indicates a condition of the observed sharp transition from the entropy-dominated to enthalpy-dominated regimes, leading to the reversal of the size-dependent sequence of elution.

In search for the CPA conditions of size-independent elution, we perform extensive DPD simulations to investigate the effects of the NP surface chemistry on NP adhesion and flow in PB-grafted pore channels in a binary solvent at different solvent composition. We consider NPs functionalized by two different types of ligands, which are modeled as short hydrophobic and hydrophilic chains grafted on the NP surface. By varying the ligand composition, we mimic different surface chemistries and control the NP-PB adhesion interaction. We analyze the specifics of solvent flow through PB-grafted channels and quantify the morphology and sorption capacity of the PB stationary phase, depending on the solvent composition by introducing the hydrodynamic PB thickness as the stationary phase boundary. The NP-PB adhesion is quantified in terms of the free-energy landscape, calculated using the Ghost Tweezers (GT) method,\textsuperscript{45} which determines the Henry constant of NP adsorption, the partition coefficient, and ultimately the NP retention time, depending on the solvent and ligand compositions. The NP retention time distribution is analyzed using the convective-diffusion model. For NP of different surface chemistry, we identified the CPA solvent composition that corresponds to a transition between the size exclusion to adsorption modes. The relationship is established between the solvent composition at CPA and the NP ligand composition that points toward a possibility of efficient NP separation by surface chemistry in the solvent gradient regime by varying the solvent composition as it is done in the gradient elution regime of interaction polymer chromatography.\textsuperscript{29,30}

The following text is structured as follows. Section II discusses the simulation models and methods which include a brief description of the DPD method, system setup, coarse-graining scheme, parametrization of the model, the ghost tweezer method, and solvent flow simulations. Section III discusses our theoretical models and results from the simulations: the calculation of free energy of NP adhesion to PB using the ghost tweezer technique from which the Henry constant and partition coefficient of NPs are derived, and the prediction of NP motion through PB-grafted channels and NP retention times based on the calculated polymer density profiles, thermodynamics calculation, and the solvent velocity profiles obtained in separate simulations. This section also discusses a macroscopic model for NP elution in a cylindrical channel in the isocratic (no solvent gradient) mode, in terms of “first passage time” distributions based on a convective-diffusion model, and the prediction of separation of our model NPs in solvent gradient elution mode of NP chromatography, utilizing the results of free-energy profiles and flow calculation, along with discussion of some practical aspects of our findings. Section IV concludes our work.

II. MODELS AND METHODS

II.I. Dissipative Particle Dynamics. DPD\textsuperscript{46–48} employs a coarse-grained (CG) scheme where atoms are lumped together into beads that interact with soft-core repulsive potentials allowing for possible overlap between the beads. In DPD simulations, the beads move according to Newton’s equations of motion governed by the pairwise interaction potentials; the total force $F_i$ on the $i$th particle is presented as

$$F_i = \sum_{j \neq i} (F_{ij}^{(C)} + F_{ij}^{(B)} + F_{ij}^{(D)} + F_{ij}^{(R)})$$

(1)

Here, $F_{ij}^{(C)} = a_{ij}(1 - \frac{r_{ij}}{R_c})\dot{r}_{ij}$ for $r_{ij} = |\mathbf{r}_i - \mathbf{r}_j| \leq R_c$, is the conservative force between beads $i$ and $j$, where $a_{ij}$ is the repulsion parameter and $R_c$ is the interaction range beyond which the conservative force vanishes; $R_c$ represents the effective diameter of the beads. The drag forces $F_{ij}^{(D)}$ and the random forces $F_{ij}^{(R)}$,

$$F_{ij}^{(D)} = -\gamma w^{(D)}(r_{ij}) (\dot{r}_i - \dot{r}_j), \quad F_{ij}^{(R)} = \sigma w^{(R)}(r_{ij}) \mathbf{\hat{r}}_{ij}$$

(2)

constitute the Langevin thermostat; $\gamma$ is the friction coefficient, $\sigma^2 = 2\gamma kT$, and $\mathbf{\hat{r}}_{ij}$ is the relative velocity between the $i$th and $j$th beads ($\mathbf{v}_i = \mathbf{v}_j - \mathbf{v}_j$). The weight functions $w^{(D)}$ and $w^{(R)}$ are...
related as $w^{(D)} = (w^{(R)})^2$, with $w^{(R)}(r_i) = (1 - r_i/R_c)$ for $r_i \leq R_c$ and $w^{(R)}(r_i) = 0$ for $r_i > R_c$. $\theta_i$ is a random variable with Gaussian statistics. In addition, the bonded beads interact via harmonic bond forces $F_{\text{bond}} = -k_{\text{bond}}(r_i - r_c)\hat{r}_i$, where $k_{\text{bond}}$ is the effective bond rigidity and $r_c$ is the equilibrium bond length.

As an instructive example, we consider a model polymer—binary solvent system consisting of polyisoprene natural rubber (PINR), benzene as a good solvent, and acetone as a poor solvent that was parametrized and studied in our previous works. We employ the most common implementation of DPD with the all beads having the same effective diameter $R_c$ = 0.71 nm. Because the persistence length of PINR in benzene—benzene solutions is very short, $\sim 2R_c$, introduction of additional bond and angle potentials is not necessary. DPD simulations are performed in reduced units with $R_c$ as the unit of length and $k_B T$ as the unit of energy with friction coefficient $\gamma = 4.5$ at a time step of 0.02 $\tau_{\text{DPD}}$, where $\tau_{\text{DPD}}$ is the unit of DPD time. Since conversion of the DPD time unit $\tau_{\text{DPD}}$ into physical units is not unequivocal, we used the experimental benzene self-diffusion coefficient ($2.21 \times 10^{-3}$ cm$^2$/s) as a reference property. Comparing the simulated value of the benzene diffusion coefficient in pure benzene ($0.22R_c^2/\tau_{\text{DPD}}$) with the experimental, we get $\tau_{\text{DPD}} \approx 50$ ps. Note that the conversion between the reduced and the real time units does not affect the elution time calculations (see Section III.1).

Simulations were performed with the LAMMPS software package. The systems contained $0.3–0.4$ million particles, and these massive parallel simulations consumed $\sim 200 \times 00$ CPU hours altogether. Configuration snapshots were created using the Visual Molecular Dynamics (VMD) program.

II.II. System Setup. PB is composed by linear chains of length $n_{\text{seg}}$ composed by P beads representing PINR monomer, which are connected by harmonic bonds. The good and poor solvent components are modeled as single beads, G and B (see Figure 1a). The G bead corresponds to one hydrophobic benzene molecule, and the B bead corresponds to one polar acetone molecule. NPs are built as spherical aggregates of radius $R_{\text{NP}}$ consisting of beads close-packed on an HCP lattice and connected by strong harmonic bonds holding the structure intact with the number density close to $3R_c^{-3}$. NPs have a core—shell structure with the shell consisting of two layers of surface N-beads that interact with solvent, ligand, and polymer beads and the core consisting of C-beads that strongly repel all other beads except for surface beads (Figure 1b). The core—shell NP structure prevents penetration of mobile beads inside the NP. We consider NPs of three different sizes with radii, $R_{\text{NP}} = 4R_c$, $6R_c$, and $8R_c$, which correspond to the NP diameters of 5.68, 8.52, and 11.36 nm, consisting of total number of beads $n_{\text{NP}} = 740, 2496$, and 5917, respectively.

The surface chemistry is modeled with “ligands”, short 6-bead long chains attached uniformly to the NP surface with strong harmonic bonds. We consider two types of ligands having distinct interaction properties, denoted as L (hydrophobic, favorably interacting with the polymer) and K (hydrophilic, unfavorably interacting with the polymer), and control the NP surface chemistry by varying the ligand composition; the degree of NP hydrophilicity is characterized by the fraction $x_K = n_K/(n_L + n_K)$ of K ligands, where $n_L$ and $n_K$ are respectively the number of L and K ligands on the NP surface.

To construct PB, polymer chains are grafted on a solid substrate that consists of densely packed immobile 5-beads with density of $19R_c^{-3}$, forming a flat surface of area $40 \times 40R_c^2$ in the $X$—$Y$ plane, as shown in Figure 1c. In most of the simulations in this work, PB is comprised of chains containing $n_{\text{seg}} = 90$ P-beads that are grafted to the substrate uniformly with the surface density of $\Gamma = 0.302S_0^{-2}$ ($0.6$ nm$^{-2}$), which

![Image](https://example.com/image.png)
Table 1. List of Repulsion and Bond Parameters of the DPD Beads in the Simulations

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<th>i/j</th>
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<th>L</th>
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represents 484 chains in total (this system is denoted below as PB1). A few selected simulations are also performed with the reduced PB density $\Gamma = 0.1806R_{\text{seg}}^{-2} = 0.36 \text{ nm}^{-2}$ and longer chain length $n_{\text{seg}} = 160$ (PB2) and with the same PB density and $n_{\text{seg}} = 200$ (PB3). The system is kept at constant density equal to the bulk solvent density $\rho_b = \rho_0 = 3R_{\text{c}}^{-3}$. The solvent quality is controlled by the fraction of the good solvent $G$-beads in the solvent, $x_G = n_G/(n_G + n_L)$, which varies in the simulations from 1% to 99%. On average, simulation systems for free-energy calculations contain $\sim 0.3$ million particles while the systems of solvent flow contain $\sim 0.4$ million particles. Altogether, we performed 1700+ simulations of $\geq 1$ million simulation steps.

**II.III. Interaction Parameters.** The interaction parameters for solvent and polymer are taken from our previous works\(^{35,44,45}\) and are presented in Table 1. The intra-component repulsion parameter $a_{ii} = 42k_BT/R_c$ for all beads, that effectively reproduces the solvent compressibility.\(^{44}\) NP core C beads strongly repel all other beads: $a_{iC} = 60k_BT/R_c$. NP surface N beads effectively attract polymer P beads, as $\Delta a_{np} = a_{np} - a_{NN} = -3.5k_BT/R_c$ ($a_{iC}/a_{ii}$ leads to an effective attraction between $i$ and $j$ bead types). The polymer P beads interact with good solvent G beads with very weak repulsion $\Delta a_{pg} = 1.5k_BT/R_c$ and are repelling poor solvent B beads with $\Delta a_{pb} = 7.0k_BT$. The hydrophobic L bead is similar to the polymer P bead with the same interaction parameters with the solvent components. The hydrophilic K beads repel P beads with $\Delta a_{kp} = 4.0k_BT/R_c$ and interact with solvent beads in the opposite manner strongly repulsive to good solvent G-beads, $\Delta a_{kg} = 5.5k_BT$, and weakly repulsive to bad solvent B beads, $\Delta a_{kb} = 1.5k_BT$. Note that the mismatch parameter between the good and poor solvents $\Delta a_{lg} = 1.5k_BT$ is determined by fitting the activity coefficient in acetone-benzene solution at ambient temperature. This choice reflects the fact that the acetone and benzene are miscible and do not phase separate to form an interface. The total density of ligands on NPs is fixed to $0.198R_{\text{seg}}^{-2}$ (0.39 nm\(^{-2}\)). To control the surface properties, the fraction of ligand $K, x_K$ is varied from 0 to 100%. All the interaction parameters are listed in Table 1.

**II.IV. The Ghost Tweezer Method.** In order to analyze the specifics of NP adhesion to PB and calculate the Henry constant and partition coefficient between mobile and stationary phases, we determine the free-energy landscape of NP adhesion to PB by the ghost tweezer (GT) method.\(^{45}\) which, in silico, mimics optical or magnetic tweezers experiments. In the GT method, NP is tethered at given position using its immobile identical twin (called the “ghost tweezer particle”) which is pinned at this point and does not interact with any other beads. NP composed of $n_{\text{seg}}$ beads is linked to GT by $n_{\text{seg}}$ inter-bead harmonic bonds connecting each NP bead with the corresponding bead in GT. GT beads are denoted as A beads, which do not interact with any system component, $a_{AA} = a_{kk} = 0$. The NP-GT inter-bead harmonic potential is weak, with a strength of $k_{GT} = 0.01k_BT/R_c^2$ (see Table 1) and equilibrium position $r_c = 0$, yet multiple bonds control NP fluctuations and prevent its rotation. Far from PB, in the absence of external forces, NP fluctuates around GT.

In the course of simulation, NP is towed by GT in Z-direction toward the substrate in small increments allowing for the system equilibration at each incremental step. When GT is placed close enough to the substrate, NP interacts with PB, the force acting on NP from PB is counterbalanced by the force exerted on NP by the GT through its $n_{\text{seg}}$ inter-bead harmonic bonds. Since the PB is symmetric in the X- and Y-directions, the average force in these directions is zero, and the force exerted by GT in normal direction, $F_{GT} = -k_{GT}\sum_{i=1}^{n_{seg}}(z_{NP}^i - z_{GT}^i)$, where $z^i$ is the distance of the ith bead from the substrate surface. Thus, one can measure the strength of NP-PB interaction by averaging the GT force, $F_{GT}(\bar{z}) = -K_{GT}(\bar{z} - Z_{GT}) = -K_{GT}\Delta z$, where $\bar{z}$ and $Z_{GT}$ are, respectively, the average center of mass Z-coordinates of NP and its GT twin, $\Delta z = (\bar{z} - Z_{GT})$, and $K_{GT}$ is the cumulative spring constant ($K_{GT} = n_{seg}k_{GT}$). Initially, when the GT is placed in the bulk solvent far enough from PB, NP fluctuates about the GT position with $\Delta z = 0$ and average NP-GT force $F_{GT} = 0$. Then, NP is pulled toward the substrate by displacing GT in successive incremental steps of $\Delta z = 0.5R_c$. The system is equilibrated at each step to measure the average NP position $\bar{z}$ and, respectively, the average force exerted by NP on PB, $F_{GT}(\bar{z})$. The free energy $A(z)$ of NP-PB interaction is the mechanical work that is required to bring the NP to the point $z$ above the substrate from the bulk, obtained by integrating $F_{GT}(\bar{z})$:

$$A(z) = \int_{z_0}^{z} F_{GT}(\bar{z}) \, d\bar{z}$$

The NP location $z_0$ far from the substrate serves as a reference point where $A = 0$.
Figure 2. (a) PB (solid lines) and binary solvent (dashed lines) density profiles along \( z \) at different solvent compositions: \( x_G = 0.01 \) (red), 0.20 (green), 0.40 (magenta), 0.60 (blue), 0.80 (black), and 0.99 (cyan). PB contracts as the solvent quality worsens. (b) Normalized (solid lines) and simulated (dashed lines) solvent velocity profiles across the channel, along with PB density profiles (diamonds) at different solvent composition: \( x_G = 0.05 \) (red), 0.10 (green), 0.50 (blue), 0.70 (magenta), and 0.90 (black). Solvent flow does not penetrate PB and is similar to the Poiseuille flow confined to the mobile phase with no-slip conditions set at the outer boundary of PB determined by the PB hydrodynamic thickness \( w_{\text{PB}} \). Simulations are at the same applied force \( g = 0.002 k_BT/R_w \) and the simulated velocity magnitude increases as the solvent quality worsens and the PB contracts. The normalized velocities represent the predicted solvent flows at the condition of the constant solvent flux. The magnitude of the normalized velocity decreases as the PB contracts and mobile phase volume increases. (c) The variation of the PB hydrodynamic thickness \( w_{\text{PB}} \) with the good solvent fraction \( x_G \). The PB hydrodynamic thickness \( w_{\text{PB}} \) represents the extension of the stationary phase.

The system setup for free-energy calculation is shown in Figure 1c, where the NP that is functionalized with short ligands is placed above PB grafted on a solid substrate. The normal dimension of the simulation box is chosen in the range of 50–56\( R_z \) to prevent overlapping of PBs on the opposite channel walls and provide NPs with enough space in the channel center to equilibrate in the bulk solvent, without hinders arising from the periodic boundary conditions. Mainly, four sets of systems corresponding to NPs having hydrophilic K ligand fraction or the degree of hydrophilicity, \( x_k = 0.25, 0.5, 0.75, \) and 1.00 are simulated. The case of NPs with entirely hydrophobic (attractive to polymer) ligands \( L \), corresponding to \( x_k = 0, \) was studied in our previous work.\(^{14}\) In each system, the free-energy landscape is calculated for NPs of three different radii \( R_{NP} \) of 4\( R_z \) (2.84 nm), 6\( R_z \) (4.26 nm), and 8\( R_z \) (5.68 nm), in solvents of different quality characterized by the fraction \( x_G \) of the good solvent component. Most simulations are performed with PB grafting density 0.6 nm\(^{-2} \) (system PB1). A few additional simulations with PBs of grafting density 0.36 nm\(^{-2} \) and polymer lengths \( n_{wG} = 160 \) (PB2) and 200 (PB3) are also performed to demonstrate the specifics of NP-PB interactions at poor solvent conditions (low \( x_G \)). The free-energy landscape \( A(z) \) is calculated at a spatial resolution of 0.5\( R_z \). Altogether, a total of \( \approx 1100 \) simulations of 1 million timesteps with 0.28–0.31 million particles are performed.

II.V. Solvent Flow Simulations. Simulations of the solvent flow are performed in the slit channel between two identical PB-grafted walls with \( Z \) being the normal and \( X \) (direction of flow) and \( Y \) being lateral directions (Figure 1d). The size of the simulation cell is 40 \( \times \) 40 \( \times \) 70\( R_z \), which corresponds to a channel width of 2\( w \approx 66.7R_z \) = 47.4 nm (subtracting the wall thickness on both sides). A steady flow is created by applying a constant force \( g \) (of magnitude \( g = 0.002 k_BT/R_w \)) to the solvent particles, at different good solvent fraction ranging from 1\% to 99\%. The solvent velocity profile across the channel \( u(z) \) is obtained by averaging over 100,000 steps after the system equilibration for 500,000 steps.

III. RESULTS AND DISCUSSION

III.I. Solvent Flow through Polymer Brush-Grafted Channels. We perform simulations of flow of binary solvent through PB-grafted slit-like channels between two identical PB-
Introduction of the hydrodynamic thickness \( w_{PB} \) allows one to define the stationary (inside PB at \( z < w_{PB} \) ) and mobile (outside PB at \( z > w_{PB} \) ) phases within the channel and to use the mobile phase volume as the reference volume for the definition of the excess NP adsorption and, respectively, the Henry constant and the partition coefficient, as described below.

It is noteworthy that the PB conformation and its hydrodynamic thickness are determined by the solvent composition and are not dependent on the magnitude of the force applied to the solvent to simulate flow and on the channel width (see Section I in the Supporting Information (SI)). This independence of the conditions of simulations implies the thermodynamic equilibrium between the solvent and PB and allows one to use the results of simulations for the channel of given width for predicting the partition coefficient and the retention time at other channel widths. The PB density \( \rho_{PB}(z, w_{PB}) \) can be considered as depending solely on the value of the hydrodynamic thickness, which is determined by the solvent composition, disregarding of the conditions of flow and the channel width. Respectively, provided the channel width \( w \) is reasonably larger than \( w_{PB} \) and the PBs of the opposite channel walls do not overlap, the solvent density can be calculated as \( \rho_s(z) = \rho_0 - \rho_{PB}(z, w_{PB}) \), as the solvent density in the bulk equals the overall bead density (\( \rho_b = \rho_0 \)).

The hydrodynamic thickness \( w_{PB} \) of PB obtained from the parabolic approximation condition (eq 4) is the main parameter characterizing the PB conformation and the solvent flow at given solvent composition. Figure 2c shows that \( w_{PB} \) is a nonlinear function of the good solvent fraction \( x_G \), which progressively increases with the addition of the good solvent and respective PB expansion.

We must compare the effects of the PB conformation at different solvent compositions on the NP adsorption and the separation at the condition of the constant flux of the solvent (\( J = \text{constant} \) ) to mimic the conditions of chromatographic experiments. Note that, regardless of the solvent composition and the respective PB conformation, the total amount of solvent in the channel cross-section is constant, \( N_s = \int_0^z \rho_s(z) \, dz = \int_0^z \rho_s \, dz(\rho_b - \rho_{PB}(z)) = \rho_b w - N = \text{constant} \). Therefore, the condition of constant flux implies that the mean solvent velocity \( \langle v_s \rangle \) also remains constant:

\[
\langle v_s \rangle = \frac{\int_0^w \rho_s(z) \, v_s(z) \, dz}{\int_0^w \rho_s(z) \, dz} = \text{constant}
\]

The simulations at different solvent compositions are performed at the same force \( g = 0.002 \) \( k_BT/R_c \) applied on the solvent particles to create a steady flow. As a result, the simulated velocity magnitude and, respectively, the solvent flux increase as the solvent quality worsens, since the PB contracts, mobile zone outside PB widens, and the resistance to the flow decreases. In order to fulfill the condition of the constant mean solvent velocity and predict the flow at a given solvent flux from the simulation performed at a certain applied force, it is convenient to operate with the normalized velocity \( v_c(z) \) reduced by the mean flow velocity,

\[
v_c(z) = \frac{v(z)}{\langle v_s \rangle}
\]

The use of the normalized velocity \( v_c(z) \) secures the equal flux condition eq 4 that is necessary for comparison of different separation regimes.

In the parabolic approximation, the normalized velocity \( v_c^{PA}(z) \) is presented in the form

\[
v_c^{PA}(z) = \chi^{-1} \left[ 1 - \frac{(w - z)^2}{(w - w_{PB})^2} \right]
\]

Here, \( \chi \) is the ratio of the mean flow velocity to the maximum velocity, under given conditions, which is dependent on the PB hydrodynamic width \( w_{PB} \) and the channel width \( w \) as

\[
\chi(w_{PB}, w) = \frac{2}{3N_s} \rho_{\text{bulk}}(w - w_{PB}) - \frac{1}{N_s} \int_{w_{PB}}^w \rho_{PB}(z, w_{PB}) \left[ 1 - \frac{(w - z)^2}{(w - w_{PB})^2} \right] dz
\]
hydrophilic ligands. The hydrophilic toward a lower solvent composition with the NP hydro-
quality facilitates adsorption, but to a lower extent, in comparison with NPs without hydrophilic ligands. At
x \approx 0.4 and the transition around x_G = 0.5 lower by 40%, compared to the case of NPs with no K ligands.

With the most hydrophilic NPs, the adsorption regime occurs only at very low solvent qualities, at x_G < 10% (see
Figure S4c in the SI). Even at x_G = 0.2, the repulsion dominates and strengthens with NP size. At x_G = 0.01, the
lowest solvent quality considered, the strength of adsorption does not increase monotonically with NP size. At these low
good solvent fractions, the poor solvent has a tendency to wrap around the NP due to the solvation by K ligands and hinder the
contact of polymers with NP surface. In addition, the completely collapsed PBs become impenetrable as the PB density becomes equal to the bulk density with a very sharp interfacial region with the bulk solvent. As a result, larger NPs cannot penetrate into PB and the number of PB-NP contacts and, respectively, the strength of adhesion does not increase with the NP size. For these reasons, a complete transition from repulsion to attraction regime with the reversal of order is not observed. Figure 3 also shows that the repulsion to attractive transition is sharper for more hydrophobic particles: the range of x_G where the transition occurs widens with increase of x_K.

To demonstrate the effects of the PB density and chain length on NP adhesion, selected simulations are also performed with two other characteristic PB systems denoted as PB2 (grafting density of 0.36 nm\(^{-2}\) and chain length \(n_{seg} = 160\)) and PB3 (same grafting density and \(n_{seg} = 200\)). The respective force and free-energy profiles of NP adhesion at x_G = 0.01 with x_K = 1.0 are given in Section III in the SI. The NP size dependence of the adsorption strength is found to be nonmonotonic for PB2, as in the case of x_K = 1.0 for the system PB1, and monotonic for PB2 within the NP size range under consideration. Since PB2 has the lower grafting density compared to PB1 and the shorter chain length than PB3, PB2 should be more flexible and penetrable for NPs than PB1 and PB3.

III.III. Excess NP Adsorption and Henry Constant. The free-energy landscape \(A(z)\) determines the probability of NP to be at a specific distance \(z\) from the substrate that is proportional to the Boltzmann factor, \(\exp(-A(z)/k_B T)\). Respectively, the NP density distribution is presented as

\[
\rho_{NP}(z) = \rho_{NP}^b \exp\left(-\frac{A(z)}{k_B T}\right)
\]

where \(\rho_{NP}^b\) is the NP density in the bulk solvent. As shown above, \(A(z)\) is dependent on the PB conformation that is determined by the solvent composition and is independent of the solvent flow and the channel width, provided that the latter sufficiently exceeds the PB width. Equation 9 allows one to calculate the Henry constant and the partition coefficient between the mobile and stationary phases. The stationary phase boundary is defined by the PB hydrodynamic thickness, \(w_{PB}\).

Division of the pore volume using the PB hydrodynamic thickness \(w_{PB}\) into stationary (inside PB at \(z < w_{PB}\)) and mobile (outside PB at \(z > w_{PB}\)) phases allows us to unambiguously introduce the NP excess adsorption (\(N_{ex}\)) as the difference between the total amount of NPs per unit substrate surface area (\(N_{tot}\)) and the amount of NPs in the reference volume of bulk solution equal to the volume of the mobile phase.\(^{53}\)
above (Figure 3). As shown in the insets where this transition occurs at lower solvent quality, as discussed particles attracted stronger. As the NP hydrophilicity increases, particles repelled stronger, to the adsorption mode, with larger size exclusion mode of negative excess adsorption with larger increases with the NP size. For all systems considered, a worsens and NPs adsorb strongly to PB, the Henry constant tendency to decrease with NP size, while, as the solvent quality and equal to the NP radius, $K_{0.75}$ is given in Figures 4a.

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Figure 4. Logarithm of Henry constants of excess adsorption of NPs with different sizes and degree of hydrophilicity. (a) $x_G = 0$ (ref 33), (b) $x_G = 0.25$, (c) $x_G = 0.5$, and (d) $x_G = 0.75$ at different solvent composition $x_C$. To avoid log of negative values of $K_{i j}$ (in nm), a constant of 10 nm is added. Inset shows Henry constant values in the size exclusion mode and the transition region. The red curves indicate NPs of radius $8R_w$ while green and blue indicate $R_{NP} = 6R_w$ and $4R_w$ respectively.

$$N_{ex} = N_{tot} - \rho_{NP}(w - w_{PB})$$

$$= \rho_{NP} \int_0^w \exp \left( - \frac{A(z)}{k_BT} \right) dz - \rho_{NP}(w - w_{PB})$$

Accordingly, the Henry constant of excess adsorption is given by

$$K_{Hex} = \frac{N_{ex}}{\rho_{NP}} = \int_0^w \exp \left( - \frac{A(z)}{k_BT} \right) dz - (w - w_{PB})$$

$$= w_{PB} + \int_0^w \left[ \exp \left( - \frac{A(z)}{k_BT} \right) - 1 \right] dz$$

The above definition of the NP excess adsorption implies that, in the case of hydrodynamic chromatography (HDC) in the channels with hard walls in the absence of PB ($w_{PB} = 0$), the excess adsorption is negative, reflecting the exclusion of NPs from the near-surface layer of thickness equaled the NP radius $R_{NP}$. Respectively, the Henry constant ($K_{Hex}^{NP}$) is negative and equal to the NP radius, $K_{Hex}^{NP} = -R_{NP}$, which reflects a stronger repulsion of larger NPs.

The dependence of the excess adsorption Henry constant, $K_{Hex}^{NP}$, on the solvent quality for NPs of different size ($R_{NP} = 4R_w$, $6R_w$ and $8R_w$) and degree of hydrophilicity $x_G = 0$, 0.25, 0.5, and 0.75 is given in Figures 4a–d. For convenience, logarithms of $K_{Hex}^{NP}$ with addition of a constant (equal to 10 nm) are plotted, to avoid negative values at the repulsive good solvent conditions. While $K_{Hex}^{NP}$ is relatively small and negative (approximately equal to $-R_{NP}$) when the NP-PB interaction is repulsive, it increases exponentially as the NP adsorption becomes stronger. At the solvent compositions where NP-adsorption is weak, $K_{Hex}^{NP}$ has a tendency to decrease with NP size, while, as the solvent quality worsens and NPs adsorb strongly to PB, the Henry constant increases with the NP size. For all systems considered, a transition is observed, as the solvent quality worsens, from the size exclusion mode of negative excess adsorption with larger particles repelled stronger, to the adsorption mode, with larger particles attracted stronger. As the NP hydrophilicity increases, this transition occurs at lower solvent quality, as discussed above (Figure 3). As shown in the insets where $K_{Hex}^{NP}$ near the transition and the size exclusion regime are depicted, this transition occurs in a narrow range of $x_G$, for NPs of given surface hydrophilicity, regardless of their size, and one can identify the characteristic "critical" condition reminiscent to the critical point of adsorption (CPA) in polymer chromatography. The dependence of such critical transition solvent quality on the NP hydrophilicity is discussed below.

III. IV. Absolute Adsorption and Partition Coefficient. While the excess adsorption allows for a rigorous thermodynamic consideration of NP adhesion, in order to analyze the NP separation in the solvent flow, one must identify the amount of retained or immobile NPs or, in other words, define the absolute adsorption. Following the conventional assumption of the hydrodynamic chromatography and assuming that NPs, which are located within distance $z < w_{PB} + R_{NP}$ from the substrate and partially immersed into PB, are immobile, the absolute adsorption is defined as

$$N_{ads} = \rho_{NP} \int_0^{w_{PB} + R_{NP}} \exp \left( - \frac{A(z)}{k_BT} \right) dz$$

Respectively, the Henry constant of absolute adsorption is defined as the ratio of the number NPs retained in the PB stationary phase (at $z < w_{PB} + R_{NP}$) per substrate unit area to the NP bulk concentration,

$$K_H = \int_0^{w_{PB} + R_{NP}} \exp \left( - \frac{A(z)}{k_BT} \right) dz$$

$$= \int_0^{w_{PB} + R_{NP}} \left[ \exp \left( - \frac{A(z)}{k_BT} \right) - 1 \right] dz + w_{PB} + R_{NP}$$

The Henry constant of absolute adsorption ($K_H$) differs from the Henry constant of excess adsorption ($K_{Hex}^{NP}$) and is always non-negative. In the size exclusion mode, $K_H \equiv K_{Hex}^{NP} + R_{NP}$. This approximate equality holds when the PB has a sharp boundary at $w_{PB}$, so that $A(z)$ is negligibly small beyond $w_{PB} + R_{NP}$. Note that, in the case of hydrodynamic chromatography in hard wall channels without PB coating, $A(z) = \infty$ at $z < R_{NP}$ and the absolute adsorption Henry constant vanishes, $K_H = 0$, in contrast to the excess adsorption Henry constant being negative, $K_{Hex}^{NP} = -R_{NP}$. The difference between absolute and excess NP adsorption is discussed in detail in Section IV in the SI.

Although the Henry constant (eq 13) is determined in the free-energy simulations performed in the channel of a particular width, this thermodynamic quantity is not dependent on the system size, provided that it is larger than the simulated system.

The partition coefficient in liquid chromatography is generally defined as the ratio of the solute concentration in
the immobile stationary phase to the solute concentration in the mobile bulk phase. However, in the system considered here with the PB stationary phase and highly inhomogeneous NP distribution at the PB-solvent interphase, it is more practical to define the apparent partition coefficient \( K_{NP} \) as the ratio of the total amount of NPs retained in the PB stationary phase at \( z < w_{PB} + R_{NP} \) and the amount of NP in the bulk mobile phase of width \( (w-w_{PB} - R_{NP}) \).

\[
K_{NP} = \frac{K_H}{(w-w_{PB} - R_{NP})}
\]

(see Section IV in the SI). In contrast to the Henry constant \( K_H \) that has the dimension of length, the partition coefficient \( K_{NP} \) is dimensionless. \( K_{NP} \) characterizes the fraction of retained NPs in the pore of given width \( w \).

The partition coefficient defined by eq 14 is calculated as a function of the good solvent fraction for NPs of different sizes and surface hydrophilicities characterized by \( x_p \). The results are shown in Figures 5a-d, which present the logarithm of \( K_{NP} \) as a function of the solvent quality \( x_p \) for NPs of different hydrophilicity (\( x_p = 0.0, 0.25, 0.5, \) and 0.75) and size \( (R_{NP} = 4R_c, 6R_c, \) and \( 8R_c \)) in the channel of \( w = 70.43R_c = 50 \) nm. In all cases, the partition coefficient monotonically decreases with increases in the nonmonotonic dependence of the solvent quality from adsorption mode to size exclusion mode. The transition from one mode to another occurs at different solvent composition for NPs with different surface hydrophilicity. This should be expected, given the \( A(z) \) and \( K_H \) depicted in Figures 3 and 4. However, the partition coefficient depends on the channel width \( w \), while the Henry constant is independent of it. The CPAs obtained from values of \( K_{NP} \) corresponding to the transition shown in Figure 5 are discussed below.

Note that, for NPs functionalized solely by hydrophilic ligands, \( x_p = 1 \), the NP-PB partition coefficient \( K_{NP} \) may be nonmonotonic, with respect to the NP size at certain PB density and chain length. As shown in Section III in the SI, such nonmonotonic dependence is related to the fact that adsorption of hydrophilic NPs may occur only at very low solvent qualities (Figure 3c), because of PB-ligand repulsion and solvation of K ligands by the poor solvent. This shows that critical conditions may not be observed in all systems.

III.V. Critical Conditions of Size-Independent NP Elution. The introduction of the PB hydrodynamic thickness \( w_{PB} \) that identifies the boundary between the stationary and mobile phases makes it possible to model NP adhesion and flow in wider channels based on the simulation data obtained in a channel of a particular width. To this end, we employ the approximate model of NP transport accepted in the hydrodynamic chromatography.\(^{52-54}\) The velocity of NPs located in the mobile phase beyond the exclusion volume boundary, \( w_{PB} + R_{NP} \), is assumed equal to the solvent velocity, while the velocity of NPs located inside this boundary is zero. Within the parabolic approximation (eq 7), the normalized (with respect to the mean solvent velocity) velocity of the NP located at the distance \( z \) from the substrate, \( v_p(z) \), is presented as

\[
v_p(z) = \begin{cases} \frac{v_{PA}(z)}{v_s} & \text{for } w_{PB} + R_{NP} < z \leq w \\ 0 & \text{for } 0 \leq z \leq w_{PB} + R_{NP} \end{cases}
\]

(15)

The hydrodynamic approximation implies that NP is effectively adsorbed and immobile if it is immersed into PB even partially with its center located at \( z < w_{PB} + R_{NP} \) that is consistent with the definition of the absolute adsorption and the Henry constant given by eq 13.

For a comparative analysis, the solvent retention time, which is defined as \( t_\rho = L/(v_s) \) and is kept constant, where \( L \) is the length of the chromatographic column, is taken as the reference and the NP retention time \( t_p \) is presented in dimensionless units:

\[
t_p = \frac{t_p}{t_s} = \frac{1}{\langle v_p \rangle}
\]

(16)

Here, \( v_p \) is the mean normalized velocity of NPs that is given by the convolution of the NP normalized velocity (\( v_p(z) \)) and the probability of the NP location at distance \( z \) from the substrate:

\[
\langle v_p \rangle = \frac{\int_0^w \exp(-A(z)/k_B T) v_p(z) dz}{\int_0^w \exp(-A(z)/k_B T) dz}
\]

(17)

Equation 17 can be simplified further assuming that \( A(z) \approx 0 \) in the entire region of mobile phase at \( z > w_{PB} + R_{NP} \) and respectively, the concentration of NP in the mobile phase can be substituted by the bulk concentration. In this case,

\[
\langle v_p \rangle \approx \frac{\int_{w_{PB} + R_{NP}}^w v_p(z) dz}{K_H + (w - w_{PB} - R_{NP})} = \frac{v_s}{1 + K_{NP}}
\]

(18)

Here, \( v_s \) is the normalized mean velocity in the limiting hydrodynamic regime of purely repulsive (i.e., with \( K_H = 0 \)) NPs, that is related to the ratio \( \lambda = R_{NP}/(w - w_{PB}) \) of the NP radius \( R_{NP} \) to the half width of the mobile phase, as

\[
v_s = \frac{1}{3} \left( 1 + \lambda - \frac{\lambda^2}{2} \right)
\]

(19)

where the factor \( j \) is defined by eq 8. Detailed derivation of the above equation is given in Section V in the SI.
Equations 16–19 provide the sought-after relationship between the retention time and the NP size and partition coefficient for given solvent composition:

$$\tau_p = \frac{1}{\langle v_p \rangle} = \frac{1}{1 + K_{NP}} \tau_i$$  \hspace{1cm} (20)

where $$\tau_i = 1/\nu_i$$ is the minimum retention time of purely repulsive NPs in the hydrodynamic regime. This relationship combines the size exclusion effects characterized by $$\tau_i$$ and the NP-PB interaction effects characterized by the partition coefficient $$K_{NP}$$.

Figure 6a presents the mean NP velocity in a slit-like channel, normalized with respect to the volumetric solvent flow, assuming parabolic approximation within a channel of width 100 nm ($$w = 70.43 R_c$$), as a function of the solvent quality for NPs of different size ($$R_{NP} = 4 R_c, 6 R_c, 8 R_c$$) and degrees of hydrophilicity ($$x_K = 0.0, 0.25, 0.5, \text{and} 0.75$$). $$\langle v_p \rangle$$ values are calculated using eq 18 for a range of $$x_G$$ with a resolution of 0.001, by interpolating and extrapolating the $$K_H$$ values between and beyond the simulated data points. For $$x_K = 0$$, the $$K_H$$ values are further smoothed. In all cases, the NP velocity $$\langle v_p \rangle$$ decreases as $$x_G$$ decreases starting from the hydrodynamic limit, first, rather slowly at high solvent quality and then more sharply near the CPA transition point. In all the four cases, $$\langle v_p \rangle$$ reverses the order of its dependence on NP size as $$x_G$$ decreases, while going from a size-exclusion mode, where $$\langle v_p \rangle$$ increases with NP size, to the adsorption mode, where $$\langle v_p \rangle$$ decreases with NP size and eventually diminishes to zero due to strong adsorption. Note that the transition becomes sharper as the NP size increases. This reversal occurs in compliance with the reversal of the thermodynamic partition coefficient at the CPA transition conditions.

Figure 6b presents the relative retention time $$\tau_p$$, as a function of the solvent quality ($$x_G$$) for NPs of different hydrophilicities ($$x_K = 0.0, 0.25, 0.5$$, and 0.75). The relative retention time decreases as the solvent quality increases and undergoes a transition from adsorption to size exclusion mode with the reversal of the sequence of elution. While in the adsorption mode (poor solvent quality), $$\tau_p \gg 1$$, because of adsorption effects; in the size exclusion mode (good solvent quality), $$\tau_p < 1$$, since the NP mean velocity exceeds that of the solvent. The insets show enlargements of the regions around $$\tau_p \approx 1$$, where the CPA transition, at which the elution time is independent of the NP size, occurs.

The above analysis presents critical conditions of NP adsorption and separation, in three ways: (1) the thermodynamic definition of the CPA, based on the reversal of the NP size dependence of the Henry constant $$K_{HNP}$$ of excess adsorption (Figure 4), (2) the chromatographic (based on the pore volume partition on mobile and stationary phases) definition using the size independence of the partition coefficient $$K_{NP}$$ (Figure 5), and (3) the hydrodynamic definition using the mean NP velocity $$\langle v_p \rangle$$ or the retention time $$\tau_p$$ (Figure 6). While the thermodynamic definition of CPA is dependent on the PB characteristics and NP surface chemistry and is independent of the channel width, the other two CPAs are dependent on the width of the channel, by virtue of eqs 14 and 18. However, it turns out that the dependence of CPA on channel width is negligible for range of channel widths...
Figure 7. NP critical point of adsorption calculated by three definitions: From the equality of thermodynamic Henry constant of excess adsorption $K_{H}^\ast$ (red), from the NP partition coefficient ($K_{NP}$) in a channel of half width 50 nm (blue) and the equality of mean NP velocities (green).

The CPA values defined by different methods are practically similar within the accuracy of our simulations. CPAs obtained from the equality of $K_{H}^\ast$ (red points) are slightly different from that of other two methods for $x_{K} = 0.25$ and 0.5; however, the deviations are small and can be attributed to the fact that, unlike that observed in the other two cases, $K_{H}^\ast$ is calculated not requiring that $A(z) = 0$ for $z > w_{NP} + R_{NP}$. From the reversal regions of the partition coefficient, $x_{K} = 0.90 \pm 0.01$ for the case of $x_{K} = 0$, while for $x_{K} = 0.25$, the transition appears to occur at a solvent composition of $x_{K} = 0.87 \pm 0.01$. For higher hydrophilicities, $x_{K} = 0.77 \pm 0.01$ at 50% hydrophilic ligand fraction $x$, which is $13\%$ lower than the completely hydrophobic particles and $x_{K} = 0.47 \pm 0.015$, for 75% K ligands, which is $48\%$ smaller. These values remain practically the same as the CPA values obtained by the equality of the mean NP velocities. Regardless of the method, the estimated CPA is strongly and nonlinearly dependent on the NP surface chemistry. Although the CPA values were estimated just for four distinct fractions of hydrophilic ligands, the interpolated $x_{K} = x_{K}$ dependence can be used to predict the critical adsorption conditions for NP of intermediate hydrophilicity.

**III.VI. Macroscopic Model of Elution Time Distribution in the Isocratic Regime.** Our simulations suggest that PB conformation characterized by the hydrodynamic width and NP adhesion characterized by the Henry constant are determined by the solvent composition and are independent of the solvent flow rate and the pore size. Further assumption that the solvent flow can be approximated by the parabolic velocity profile beyond the PB hydrodynamic width makes it possible to predict NP elution in the channels of arbitrary size based on the simulations performed in a particular pore geometry with dimensions smaller than those of practical chromatographic supports.

Let us consider the elution time distributions in PB-grafted channels of cylindrical shape, which is a conventional model representation of the pore space geometry in separation media in hydrodynamic chromatography. When the channel radius $w$ is sufficiently large, the surface curvature effects can be neglected and the PB conformation and NP adhesion can be characterized by the same hydrodynamic width $w_{NP}$ and Henry constant as simulated in the slit-like channel of a smaller width. Accordingly, we further assume that, in a PB-grafted cylindrical channel, the solvent flow in the mobile phase (at $r \leq w - w_{NP}$) is approximated by the Poiseuille profile in the cylindrical tube of radius $w - w_{NP}$:

$$v_s(r) = 2\bar{v} \left[ 1 - \frac{r^2}{(w - w_{NP})^2} \right]$$

(21)

where $\bar{v}$ is the mean velocity of the solvent in the mobile phase and $r$ is the radial coordinate. Like in the case of the slit-like channel, we define the mean solvent velocity across the channel,

$$\langle v_s \rangle = \frac{\int_{0}^{w-w_{NP}} \rho_s(r) v_s(r) dr}{\int_{0}^{w} \rho_s(r) dr} = 2\bar{v} \chi_s$$

(22)

Equation 22 implies the cylindrical symmetry of the distributions of solvent and PB densities, $\langle \rho_s = \rho_s(r) ; \rho_{PB} = \rho_{PB}(r) \rangle$. The dimensionless factor $\chi_s$ is given by

$$\chi_s = \frac{\int_{0}^{w-w_{NP}} \rho_s(r) \left[ 1 - \frac{r^2}{(w - w_{NP})^2} \right] dr}{\int_{0}^{w} \rho_s(r) dr}$$

(23)

The normalized velocity of the solvent equals $v_s(r) = v_s(r) / \langle v_s \rangle = \chi_s^{-1}(1 - r^2 / (w - w_{NP})^2)$, which means that the mean normalized solvent velocity $\langle v_s \rangle = 1$. As such, $\chi_s^{-1}$ represents the maximum normalized solvent velocity.

To estimate the distribution of elution time due to axial dispersion of NP along the column due to the nonuniform (Poiseuille-like) solvent flow, we employ the First Passage Time (FPT) distribution model\(^{56-57}\) that implies an equilibrium distribution of NPs between the mobile and stationary phases characterized by the apparent partition coefficient $K_{NP}$ (eq 14), which, for cylindrical channel, takes the following form:

$$K_{NP} = \frac{K_{NP} S}{V_m} = \frac{2K_H}{w - w_{NP} - R_{NP}}$$

(24)

Here, $S = 2\pi (w - w_{NP} - R_{NP}) L$ and $V_m = \pi (w - w_{NP} - R_{NP})^2 L$ are the surface area and the volume of the core of the channel of radius $z = w - w_{NP} - R_{NP}$ and length $L$, available for unretained NPs. The FPT model presents the elution time distribution in the form of the inverse Gaussian distribution, which, in the dimensionless variables of time, reduced to the solvent retention time $\tau$ and the axial length reduced to column length $L$, takes the form\(^{56,57}\)

$$g(\tau) = \frac{1}{\sqrt{4\pi \bar{E}_{NP}^2}} \exp \left[ - \left( \frac{1 - \tau / \tau_{0}}{4\bar{E}_{NP}^2} \right)^2 \right]$$

(25)

where $\bar{E}_{NP}$ is the reduced longitudinal (axial) dispersion coefficient, $\bar{E}_{NP} = E_{NP}^2 / L^2$. The detailed derivation of eq 25 is given in Section VI in the SI.

In the purely hydrodynamic limit ($A(z) = 0$), the mean NP velocity in the channel is found to be (see Section VII in the SI)

$$\langle v_p \rangle = \frac{\chi_{NP}^{-1}}{2} (1 + 2\lambda - \lambda^2) = \bar{v}_0 v_p$$

(26)

where $\bar{v}_0 = \chi_{NP}^{-1}/2$ is the mean velocity of solvent in the mobile phase. Note that $\bar{v}_0$ is different from the mean solvent velocity.
\( \langle v_n \rangle = 1 \), because of the stagnant solvent inside the PB immobile phase. Note that eq 26 was suggested for NP flow in channel with solid walls, and the existence of the PB may invoke additional effects such as NP rotation that cause them to move with a velocity lower than the local solvent velocity.\(^53,58\) However, these effects should be analyzed, and the existing approximate approaches are limited to solid particles in hard wall channels. In the case when NP adsorption is present, following the existing methodology,\(^59\) it can be shown that (see Section VII in the SI)

\[
\langle v_n \rangle = \frac{\psi_{ij}}{(1 + K_{NP})}
\]

Thus,

\[
\tau_p = \frac{1}{\langle v_n \rangle} = \frac{(1 + K_{NP})}{\psi_{ij}} = (1 + K_{NP})\tau_j
\]

where \( \tau_j \) is the NP retention time in the hydrodynamic (no adsorption) limit in a cylindrical channel of radius \( w - w_{PB} \). The major contribution to the NP dispersion comes from the convective dispersion characterized by the Taylor–Aris\(^60,61\) axial dispersion coefficient \( E_{NP} \). The \( E_{NP} \) dependence on the NP size and the partition coefficient can be incorporated following the works of Brenner and co-workers\(^5,59,62\) (see Section VII in the SI)

\[
E_{NP} = \frac{D_{NP}^2}{48}\left(w - w_{PB}\right)^2\left(1 - 1.8622 + 9.68d^2\right)\frac{1 + 6K_{NP} + 11K_{NP}^2}{(1 + K_{NP})^3}
\]

Here, \( D_{NP} \) is the NP diffusion coefficient related to the NP radius through the Stokes–Einstein equation. In eq 29, the polynomial dependence on \( \lambda \) was obtained by Brenner and Gaydos\(^53\) from considerations of hydrodynamic effects on the particle motion and diffusion in a cylindrical pore with smooth hard walls and spherical NPs. A detailed derivation of eq 29 is given in Section VII in the SI.

Figure 8 presents the calculated isocratic elution time distributions for NP separation in the PB-grafted cylindrical channel of radius \( w = 50 \text{ nm} \) at different solvent conditions. The values of the partition coefficient \( K_{NP} \) the maximum normalized solvent velocity \( \chi_{r,1} \) and the PB hydrodynamic thickness \( w_{PB} \) are obtained as functions of the solvent quality \( x_G \) by the appropriate interpolation and extrapolation of the data given in Figure 6. The value of the column length \( L = 4.7 \times 10^7 R_c \) (3.34 cm) is taken to get the distinct distributions, (see Section VII in the SI, for more details) Figures 8a–d shows elution distributions for NP of different hydrophobicity, \( x_K = 0.0, 0.25, 0.5 \) and \( 0.75 \) at different solvent composition \( x_G \). Transition from the size-exclusion (left column) and adsorption (right column) regimes with the reversal of the sequence of elution occurs as \( x_G \) decreases and the solvent quality worsens. The central column shows the CPA conditions of size-independent elution.
where the elution time distributions for NPs of different size overlap with insignificant deviation of the retention times. When the solvent quality is reduced further, the retention times increase dramatically in the adsorption mode, with the reversed order of elution. Noteworthy, the CPA conditions of size-independent NP elution found at the distinct values of solvent composition (0.90, 0.86, 0.77, and 0.47) depending on the NP surface chemistry ($x_K = 0.25, 0.5,$ and $0.75,$ respectively), which within the accuracy of our simulations correspond to the same estimates shown in Figure 7.

III.VII. NP Separation in the Gradient Mode of Elution.

In interaction polymer chromatography, the gradient elution with temporal variation of the solvent composition is found to be more efficient in separating polymers according to their chemical composition than the isocratic elution. In the linear gradient mode, $x_{Gi} = x_G^0 + at$, where $x_G^0$ is the initial solvent composition at $t = 0$ and $a = dx_G/dt$ is the solvent composition gradient that is kept constant. The gradient mode of elution is based on the strong dependence of the elution time $t_p$ on the solvent composition $x_{Gi}$ in the isocratic mode, $t_p = t_p(x_{Gi})$. Let us assume that the solute components of different chemistry can be in a range, with respect to the solvent compositions ($x_G^0$), corresponding to their CPA conditions in the isocratic mode. This means that the retention time $t_p$ for a particular component sharply reduces in the vicinity of the respective CPA solvent composition $x_{Gi} = x_G^0$ from long retention times in the adsorption regime at $x_{Gi} < x_G^0$ to much shorter times in the size exclusion regime at $x_{Gi} > x_G^0$. In the gradient elution mode, one starts with a mobile phase composition $x_{Go}$ in which all solute components are adsorbed strongly to the stationary phase, so that the retention times are longer than the time of experiment. This implies that the initial composition is beyond the range of the CPA solvent compositions of all the components, $x_G^0 < x_{Gi}$. Then, the solvent composition is varied, keeping the solvent volumetric flow constant; $x_{Gi}$ gradually increases and the solute fractions desorb from the stationary phase and elute with respect to their CPA solvent compositions. The solute fraction of given chemistry desorbs and start moving once $x_{Gi}$ approaches the respective value of $x_G^0$ with a small difference in “take-off” times, $t_i$, around $(x_G^0 - x_{Gi})/a$, for the fraction components of different size, which eventually elute within a relatively narrow range of retention times. As a result, the fractions of different chemistry are separated with a minimal deviation of the retention times, which necessarily arises due to the difference in size and effects of longitudinal dispersion.

The theory of the gradient elution relates the mean retention time $t^*_{Gi}$ of a particular component in the gradient mode to the isocratic retention time $t_p(x_{Gi})$ that is a known function of the solvent composition $x_{Gi}$. Assuming that the solvent composition is varied over time, according to a certain function $x_{Gi}(t)$, with the solvent retention time $t_i$ kept constant, the mean retention time $t^*_{Gi}$ in the gradient mode is calculated from the following integral equation:

$$
\int_0^{t_i-t_i} \frac{df}{t_p(x_{Gi}(t)) - t_i} = 1
$$

(30)

A detailed derivation of eq 30 is given in Section VIII in the SI.

Extending the FPT model, the retention time distribution in the gradient mode can be estimated by the shifted inverse Gaussian distribution,

$$
g(t) = \frac{1}{\sqrt{4\pi E_{NP}(t - t_i)^3}} \exp \left\{ -\frac{1 - (\tau - t_i)/(t_i^2 - t_i)^2}{4E_{NP}(t - t_i)} \right\}
$$

(31)

Equation 31 is written using the dimensionless time $(\tau = t/t_i)$ and all temporal parameters are reduced with respect to the solvent retention time $t_i$. Here, $t_1 = t_i/t_i$ is the reduced “take-off” time and $E_{NP}$ is the reduced dispersion coefficient for given component. Note that the “take-off” time $t_i$ is defined from the expert assumption that $x_{Gi}(t_i) = x_{Gi}(t_i)$ corresponds to the solvent composition at which given component desorbs from the stationary phase. The dispersion coefficient is calculated according to eq 29 at the solvent composition close to $x_{Gi}$, $E_{NP} = E_{NP}(x_{Gi})$.

Figure 9 depicts the inverse Gaussian distributions given by eq 31 during the gradient elution of NPs with different sizes and surface chemistry $x_K$ in a cylindrical channel of radius $w = 70.43R_c$. To obtain these profiles, we set $dx_G = 0.0002$ and $df = 0.02$ (rate of composition change given as $\frac{dx_G}{df} = 0.01$) while the elution starts with a solvent composition $x_G^0 = 0.3$. The black line shows the change in solvent composition in the course of elution. The NPs of sizes $R_{NP} = 4R_c$, $6R_c$, and $8R_c$ and surface chemistry $x_K = 0.75$, $0.5$, $0.25$, and $0$ are in the middle phase in equal proportions. The takeoff composition for each NPs in each case of $x_K$ is taken according to the velocity curves, at a point where the NP starts moving, different for different NPs. The distributions are calculated for NP velocities smaller than the solvent velocity (see Section VIII in the SI).

As shown in the Figure 9, the NPs elute with retention times that are dependent on their degree of hydrophobicity in the reverse order. The retentions times are well-separated, according to their degree of hydrophilicity in the gradient mode of elution. Note that the separation efficiency is
affected by the broadness of the NP size distribution. Here, we model relatively small NPs several nanometers in diameter within a relatively narrow size range. The quality of separation would worsen if the size distribution were broader. NPs considered in this work are functionalized by hydrophobic and hydrophilic ligands with relatively weak interaction potentials that do not include any specific intermolecular interactions with polymer and solvent (e.g., dissociation with formation of charged groups).

IV. CONCLUSIONS

We considered separation of NPs functionalized by different types of ligands in PB-grafted channels, by varying the binary solvent composition and confirmed our hypothesis about the existence of critical point of adsorption (CPA) in such systems. The CPA is defined as the particular solvent composition, which corresponds to the transition between the size exclusion and adsorption modes and is dependent on the NP surface chemistry. Note that in contrast to polymer adsorption, the introduced CPA of NP adhesion to PB is not related to any critical phenomenon; rather, it indicates a condition of the observed sharp transition from the entropy-dominated to the enthalpy-dominated regimes, leading to the reversal of the size-dependent order of elution. Extensive DPD simulations are performed to investigate the effects of the NP surface chemistry on NP adhesion and flow in PB-grafted pore channels in binary solvents of different composition. We considered NPs functionalized by two different types of ligands, which are modeled as short hydrophobic and hydrophilic chains grafted on the NP surface. By varying the ligand composition, we mimic different surface chemistries and control the NP-PB adhesion interaction. We analyze the specifics of solvent flow through PB-grafted channels and quantify the conformation and sorption capacity of the PB stationary phase, depending on the solvent composition, by introducing the hydrodynamic PB thickness as the stationary phase boundary. The NP-PB adhesion is quantified in terms of the free-energy landscape calculated using the ghost tweezers (GT) method, which determines the Henry constant of NP adsorption, the partition coefficient, and, ultimately, the NP retention time, depending on the solvent and ligand compositions. The distributions of NP retention time are analyzed using the convective diffusion model, in the isotropic and gradient elution modes. The relationship is established between the CPA solvent composition and the NP ligand composition that points toward a possibility of NP separation by surface chemistry in the gradient mode of elution by varying the solvent composition as it is done in the interaction polymer chromatography.

ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acsjpcc.9b01219.

Description of the simulations of the PB density and solvent flow in slit-like channels of different width (Section I); derivation of the dependence of the ratio between the mean and maximum solvent velocity of the solvent velocity profiles on solvent and polymer brush density, channel width, and PB effective height (eq 8) (Section II); dependence of the effective force between the NP and PB on NP location for different systems (Section III); description of the excess adsorption of NPs and its relevance to the partition coefficient (Section IV); the derivation the mean velocity of NP in a slit-like channel (eq 19 in the paper), giving the mean velocity in different systems (Section V); description of the elution time distributions, in terms of the first passage time (Section VI); description of the NP transport in cylindrical channels, in terms of mean velocity and the mean axial dispersion coefficient (Section VII); and the relationship between the NP mobilities in the channel and the predicted retention time distributions in the gradient elution NP chromatography (Section VIII) (PDF)

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Notes

The authors declare no competing financial interest.

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