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Transport properties and size exclusion effects in wide-pore superficially porous particles

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Abstract

The effects of hydrodynamic radius on the transport of solute molecules in packed beds of wide-pore superficially porous particles (SPP) are studied using pore-scale simulation. The free molecular diffusion rate varies with radius through the Stokes-Einstein relation. Lattice Boltzmann and Langevin methods are used to model fluid motion and the transport of an ensemble of solute molecules in the fluid, providing statistics on solute concentration, flux, molecule age and residence time, as a function of depth in the SPP. Intraparticle effective diffusion and bed dispersion coefficients are calculated and correlated with the hydrodynamic radius and accessible porosity.

The relative importance of convection and diffusion are found to depend on the molecule (tracer) size through the diffusion rate, and convection effects are more significant for larger, slower-diffusing molecules. When larger molecules are utilized, the intraparticle concentration is reduced in proportion to the local particle porosity, leading to a natural definition of the accessible porosity used in size exclusion chromatography (SEC). Although the pore shape is complex, the SEC constant K can be calculated directly from simulation. Simulation demonstrates that the effective diffusion coefficient is elevated near the particle hull, which is largely open to interstitial flow, and decreases with depth into the particle. All molecules studied here have transport access to the entire particle depth, although the accessible volume at a given depth depends on their size. The first passage time into the particle is well predicted by the diffusion rate, but residence time is influenced by convection, shortening the average visit duration. These results are of interest in “perfusion” chromatography where convection is thought to increase separation efficiency for large biomolecules.

Keywords

Superficially porous particle; Size-exclusion; Accessible porosity; Pore-scale simulation; Restricted diffusion; Residence time distribution

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1. Introduction

Wide-pore superficially porous particles (SPPs) are now being utilized as a platform for separating large biomolecules and industrial polymers using high performance liquid chromatography (HPLC) (Wagner et al., 2017). The morphology of SPPs includes an inert, nonporous solid core with an outer layer of porous material where chromatographic retention takes place. The performance and mechanism of smaller-pore SPPs relative to fully porous particles (FPPs) has been discussed in a number of publications of which a few are cited here (Gritti et al., 2007, 2010; Wang et al., 2012; Schuster et al., 2012; Hayes et al., 2014). In addition to the standard method of gradient elution chromatography, commonly used for biochemical separations, size exclusion chromatography (SEC) has recently been explored (Schure and Moran, 2017; Pirok et al., 2017; Wagner et al., 2017) using wide-pore SPPs. To improve and optimize the performance of this class of materials, the transport of solute molecules into and out of pores of these particles must be understood for both gradient elution LC and SEC.

The outermost layer of a typical wide-pore SPP is a highly porous interface between the interstitial fluid region and shell media, and constitutes a significant fraction of the shell volume (Schure et al., 2017). In SPPs, the solid core typically ranges from 60% to 80% of the particle radius. Thin shells facilitate faster mass transport between the retentive region and the interstitial region. This leads to higher chromatographic performance through less zone broadening.

A number of recent studies have examined aspects of the fundamentals of separations in porous material as a function of the solute tracer to pore size ratio, $\lambda \equiv r_{\text{mol}}/r_{\text{pore}}$. For example, Wernert et al. (2010) presented plate height data under retention-less conditions with probes of different size using silica-based columns. The data showed that zone broadening increased dramatically as λ increased. Effective diffusion was predicted using a restricted diffusion model from filtration theory (Renkin, 1954), modified with novel expressions for size-dependent porosity and tortuosity that improved the predictions for larger values of λ . The effect of molecule size in restricted diffusion is well-known from theoretical studies of pore diffusion (Brenner and Gaydos, 1977; Dechadilok and Deen, 2006; Carta and Jungbauer, 2010). In a recent study of size exclusion in silica monolithic media, Brownian Dynamics (BD) was used to evaluate effective diffusion in reconstructed media for a wide range of λ , and the results were compared with standard filtration theory (Hlushkou et al., 2017). The agreement was good for small values of λ but, like Wernert et al. (2010), they found a straightforward application of theory tended to overpredict effective diffusion for larger values of λ . Experimental and simulation results on pore diffusion were compared in Langford et al. (2006) using different media and probe sizes. BD simulations were conducted in reconstructed digital chromatographic media, and the same media were also analyzed to create network models of pore connectivity. The expected decreasing relationship between effective diffusion and probe size was observed in both simulations and experiments. Among their conclusions, the authors noted the agreement was strongest for media where structural sampling and reconstruction was most representative, e.g., where the media was more homogeneous.

A number of studies, including Koku et al. (2012) in addition to those mentioned above, have demonstrated the ability of BD to recover fundamental structural and transport properties of actual supports which have been imaged and reconstructed at the pore length scale. Similar methods are used here to quantify mass transport between SPP and the surrounding interstitial fluid in a packed bed. But in the present case, the simulated media is a random packing of model SPPs rather than reconstructed digital media. The model SPP is compared with its physical counterpart in Schure et al. (2017), along with the construction of the SPP packed media and a detailed study of fluid flow at the pore scale. The mass transport results in the present work utilize the flow fields from that study and the flow conditions are similar to those used in HPLC. The use of a well-characterized particle allows the results to be easily analyzed as a function of depth in the particles, leading to a better understanding of the size exclusion and pore diffusion mechanisms in wide-pore SPPs used in chromatography.

In the present study, identical simulations are performed using solute molecules of different radii in a single realization of a packed bed of SPPs. The calculations are computationally intensive because two important length scales must be resolved; the sol particles (shell media) and the SPP particle itself. Hence, the computational fluid dynamics grids tend to be quite large. A related factor is that BD simulations and related methods are constrained to fairly small space and time steps, and the number of steps required to explore the pore space grows inversely with the diffusion coefficient for a given solvent flow rate.

The simulation results are organized around four topics: (1) intraparticle concentration as a function of depth in the particle and molecule radius, (2) flux within the particle as a function of depth, (3) dispersion in the packed bed and (4) solute molecule residence time in the particle. The results on concentration provide a very clear picture of the size exclusion effect and reveal a relationship between the local concentration and porosity, given explicitly as a function of shell depth. The results on flux show the role of convection near the particle hull and illustrate an approach for calculating effective diffusion from the unidirectional flux of molecules through a spherical interface. The results on dispersion in the packed bed are pre-asymptotic, but illustrate the divergence between packed beds of solid versus porous particles. The results on residence time include an analysis of mean first passage time and mean age versus depth in the particle, as well as the cumulative intraparticle residence time. The practical interpretation of these results regarding biomolecule separations is discussed in the conclusion.

2. Models and methods

2.1. SPP packed bed model

The model particle consists of a solid spherical core, $r_c = 1.650 \mu\text{m}$, surrounded by a porous shell comprising a random packing of 12,209 spherical sol particles. The sol particles have radius $r_{\text{sol}} = d_{\text{sol}}/2 = 57.5 \text{ nm}$. There are approximately four layers of sol particles in the shell. The hull is defined as a bounding sphere around the shell with radius $r_h \approx 2.15 \mu\text{m}$.

The physical particle that serves as the basis for the model SPP has a mean pore radius $r_{\text{pore}} \approx 50 \text{ nm}$, which was obtained by nitrogen adsorption techniques (Schure et al., 2017). This

pore radius is on the order of the sol radius. The pore size of the model SPP varies significantly in the shell and is better represented as a range, based on the intraparticle nearest-surface distribution (NSD). The NSD is the probability density for the distance from a point in the fluid to the nearest solid surface. It has a single mode, $r \approx 0.04d_{\text{sol}}$, and ranges up to $r \approx 0.8d_{\text{sol}}$, which reflects the porous hull region. The NSD is shown in Fig. 4 of Schure et al. (2017). The model SPP porosity is described in Section 3.1 as a function of depth in the shell.

A random packing of SPPs was simulated by replacing the spheres in a random packing of solid spheres with SPPs of the same radius. The SPP random packing is shown in Fig. 1. The original packing of solid spheres was generated by a Monte-Carlo (MC) compression algorithm in a cubic bounding box using periodic boundary conditions (PBCs). The final configuration has a box dimension $L = 9.35r_h$ and porosity of 36%. After replacing the solid spheres with randomly rotated SPPs, the spaces between particles were no longer closely packed because the SPP hull is a porous boundary. The bounding box was therefore compressed by further MC iterations, reducing its dimensions by 1% or approximately $3r_{\text{sol}}$. The resulting interstitial region of the SPP bed is 34% of its bounding box volume. The total packed bed porosity, ϵ_T , is the sum of two contributions: the interstitial void space ϵ and the intraparticle void space, ϵ'_p , expressed as a fraction of total bed volume. For a solid-sphere packing, $\epsilon_T = \epsilon$. Note, ϵ'_p is not the porosity of an individual SPP (see Section 3.1) but rather the ratio of intraparticle void volume to total bed volume.

Intraparticle porosity is the void fraction in the SPP shell. The average value is $\epsilon_p^S = 0.579$.

Intraparticle porosity as a function of depth in the particle is shown in Fig. 2. $\epsilon_p^S(r)$ is the void fraction of the thin shell between two concentric spheres, $S(r)$ and $S(r + \Delta r)$, contained within the SPP shell. Δr is a small increment described below. A closely related quantity is $\phi(r)$, the fraction of $S(r)$ open to flow. Because Δr is small, $\phi(r)$ is similar to $\epsilon_p^S(r)$ over the range of r . Table 1 summarizes porosity statistics for the random SPP packing and a body-centered cubic (BCC) packing.

2.1.1. Notation for radial averages—Intraparticle quantities such as accessible porosity, concentration, flux, and age are presented as functions of radial position in the SPP shell. These radial profiles represent averages of the three-dimensional quantities calculated within thin concentric spherical shells contained within the SPP hull. The radial position is frequently referred to as the “depth” in the particle, given in dimensionless form by $(r_h - r)/d_{\text{sol}}$. The shell thickness Δr is set equal to the fluid dynamics grid spacing, Δx , which is defined below in Section 2.3.

2.2. Fluid flow

Steady, low Reynolds number flow of water under a uniform pressure gradient was simulated in the pore spaces of the SPP packed bed. The sol Reynolds number was $Re_{\text{sol}} = \bar{v}d_{\text{sol}}/\nu = 10^{-3}$, where $\bar{v}$ is the mean pore velocity and ν is the kinematic viscosity (ν

$= 10^{-6} \text{m}^2/\text{s}$) Other hydraulic parameters, including the pressure drop, permeability, and mean fluid velocity are given in Table 2.

Fluid motion in the pore space is described by the incompressible Navier-Stokes equations with appropriate initial and boundary conditions (White and Corfield, 2006). Fluid flow was simulated under the assumptions of steady, saturated flow at small Mach number using the lattice Boltzmann (LB) method. The LB method solves the discrete-velocity Boltzmann equation for the fluid mass and momentum density distributions (Sterling and Chen, 1996; Maier et al., 1998; Maier and Bernard, 2010; Krüger et al., 2016). The method is a pseudo-transient, explicit scheme for recovering Navier-Stokes behavior in the low Mach-number limit. The LB equations are solved on a regular 3-D grid with the D3Q19 method (Maier et al., 1998; Wagner, 2008; Krüger et al., 2016), in which physical space is discretized on a computational grid and velocity space is represented at each point by a set of 19 direction vectors. The computational grid is superimposed on the packed bed geometry and calculations are carried out in the fluid region of the grid.

The packed beds were created with PBCs (Section 2.1) and the same approach was used to wrap the flow around to the opposite faces of the simulation box. Since the box has no external inflow or outflow boundaries, a pressure gradient is simulated by imposing a uniform body force in the fluid, oriented along the z -axis of the simulation box. Gravitational forces were not included and no-slip boundaries conditions were enforced at all solid surfaces. The no-slip boundary condition is chosen to represent the condition of a highly wetting fluid, such as water, on a hydrophilic surface such as chromatographic silica. Slip flow (Neto et al., 2005; Voronov et al., 2006; Huang et al., 2008; Rogers et al., 2015), which is thought to occur on highly hydrophobic surfaces with hydrophilic solvents such as water, is not considered here but may lead to some degree of non-zero velocity at the particle surface when non-wetting solvent systems are employed. The flow simulation was initiated at zero velocity and iterated to a steady state. Application of the method to porous media flows and its accuracy have been evaluated in previous work (Maier and Bernard, 2010). A full description of the present flow results, including details on grid resolution, is presented in Schure et al. (2017).

The computational grids for the random and periodic SPP packings are 3D, regular grids with fluid velocity values at the grid cell centers. The grid cell size is smaller than the sol particles, $\Delta x \approx d_{\text{sol}}/24$. The number of grid cells in the SPP random pack is $4160 \times 4160 \times 4160$. The grid is divided into rectilinear subdomains which are mapped to computer processors using the MPI Cartesian communicator topology (MPI Forum, 2016). Border cell data is exchanged between adjacent subdomains at each LB time step. Only grid cells within the pore space are part of the flow calculation. The flow solutions were completed using 1024 Sandy Bridge nodes (16,384 cores or MPI processes) on the Texas Applied Computing Center stampede system during 2016–2017.

2.3. Solute transport

The transport of dilute, conservative molecular tracers was simulated in the pore space of the SPP packed bed. These molecules range in radius from 0.1375 nm, approximately half of the O-O distance in water, calculated to be 0.292 nm (Mahoney and Jorgenson, 2000), to 20% of

the sol size, $0.2r_{\text{sol}}$. The range was intended to span from almost a point source, like water, to colloidal material, which is known to encounter restrictions in separations media at $\lambda \approx 0.2$. Note that the term “molecule” denotes a hard sphere particle that does not overlap at an interface. Furthermore, these molecules possess no long or short-range forces mediated by charge, attractive forces (e.g. van der Waals forces) or repulsive forces. No hydration layer is assumed. A summary of the molecular tracers used for this study is given in Table 3.

The molecular diffusion coefficient was calculated from the Stokes-Einstein relation (Probstein, 2003):

$$D_0 = \frac{k_B T}{6\pi\eta r_{\text{mol}}} \quad (1)$$

where D_0 is the free solution molecular diffusion coefficient, k_B is Boltzmann's constant, T is absolute temperature, η is the dynamic viscosity and r_{mol} is the radius of the solute molecules. The motion of individual molecules in the pore fluid was modeled by the Langevin equation (Uhlenbeck and Ornstein, 1936; van Kampen, 1992), assuming only the influence of Brownian motion and solvent drift velocity,

$$d\mathbf{x}/dt = \mathbf{v}(\mathbf{x})dt + F(t) \quad (2)$$

where $\mathbf{x}(t)$ denotes the solute molecule position, $\mathbf{v}(\mathbf{x})$ the local drift velocity, and $F(t)$ a fluctuating force term.

The Langevin equation is solved by a forward Euler method,

$$\mathbf{x}(t + \Delta t) = \mathbf{x}(t) + \mathbf{v}(\mathbf{x}(t))\Delta t + \xi\sqrt{6D_0\Delta t} \quad (3)$$

where ξ is a random vector on the surface of the unit sphere (Kloeden and Platen, 1992). The vector $\mathbf{s}(t) = \mathbf{x}(t + \Delta t) - \mathbf{x}(t)$ denotes the step direction.

Collisions between molecules are not modeled but collisions with the solid pore matrix are a key aspect of the simulation and these are modeled as frictionless contacts. The molecule travels along $\mathbf{s}(t)$ until it contacts a solid or the distance traveled is $s = |\mathbf{s}(t)|$. At a point of contact, the molecule continues to travel in the direction $\mathbf{p}$ tangent to the surface. If it contacts another sol particle, the step direction is again modified until the cumulative distance traveled is equal to s . Rotational degrees of freedom are not modeled. Given the molecule position $\mathbf{x}$ and step $\mathbf{s}$, the sequence of calculations to advance the position is:

```
repeat
  a ← 1
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for all potential contacts  $\mathbf{y}_i$  in the neighborhood of  $\mathbf{x}$  do
  solve  $\|\mathbf{x} + \hat{\alpha}\mathbf{s} - \mathbf{y}_i\| = r_m + r_i$  for the trial step fraction  $\hat{\alpha}$ 
  if  $\hat{\alpha}$  is real and  $\hat{\alpha} < \alpha$  then
     $\alpha \leftarrow \hat{\alpha}$ ;  $\mathbf{p} \leftarrow \mathbf{s} - (\mathbf{s}^T \mathbf{n} / \mathbf{n}^T \mathbf{n}) \mathbf{n}$ , where  $\mathbf{n} = \mathbf{x} + \alpha \mathbf{s} - \mathbf{y}_i$ 
  end if
end for
 $\mathbf{x} \leftarrow \mathbf{x} + \alpha \mathbf{s}$ ;  $\mathbf{s} \leftarrow (1 - \alpha) \mathbf{p}$ 
until  $\alpha = 1$ 

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where $\mathbf{y}_i$ and $r_i, i \in \mathcal{N}$, denote the centroids and radii of the set of solid particles in the molecule's neighborhood. Potential solid contacts are identified by the standard cell list method (Tildesley and Allen, 1987). The contact cell size for this method is set to the sol diameter. When a molecule enters a cell, a standard neighbor list is computed, consisting of sol particles in the cell and its 26 neighboring cells. This list is augmented by any SPP core particles or hull boundaries that intersect the cells. A molecule typically takes many time steps in a cell, so smaller subsets of the neighbor list are computed more frequently to reduce the number of contact checks.

The value of $\mathbf{v}(\mathbf{x})$ in Eq. (3) is interpolated from the fluid velocity field. This field is a 3D regular grid with fluid velocity values at the grid cell centers. The grid cell size is smaller than the sol particles, $\Delta x \approx r_{\text{sol}}/24$, but may be larger or smaller than the molecule radius. For $r_{\text{mol}} < \Delta x$, the value of $\mathbf{v}(\mathbf{x})$ is simply the velocity of the grid cell where the molecule is located. For $r_{\text{mol}} > \Delta x$, $\mathbf{v}(\mathbf{x})$ is the average of the velocity values of all grid cell centers covered by the molecule.

The time step is calculated by solving for Δt in the equation $|\mathbf{v}| \Delta t + 6D_0 \Delta t = \Delta x$. The left-hand side of this equation is an upper bound on s from the triangle inequality and limits the step length to Δx . Because the calculation of Δt is based on the grid parameter, Δx , the accuracy of this approach depends on the grid resolution. The present simulations were not repeated to study the effects of reducing or increasing the grid resolution, but the effects were studied earlier in Maier et al. (2000) for tracer particles. There, it was found that the time-dependent dispersion coefficient simulated in a random sphere packing achieved acceptable convergence at a resolution between $d_{\text{sol}}/29.5 < \Delta x < d_{\text{sol}}/14.7$, and was well converged for $\Delta x = d_{\text{sol}}/29.5$ (Fig. 5), while in the present work, $\Delta x = d_{\text{sol}}/24$. For random sphere packs, the effect of underresolving the grid, or making the time step too large, appears to be an underestimate of dispersion (Maier and Bernard, 2010) (Fig. 17). However, other factors may come into play, including boundary conditions. For example, a long-time simulation using PBCs can overestimate dispersion if recorelation becomes significant. In summary, the present simulations are believed to employ an adequate level of resolution for the case of tracer particles. However, the use of finite-size molecules introduces many additional and related questions regarding the simulation of Brownian motion in the presence of boundaries, and further investigation of these numerical issues is needed.

2.4. Dispersion

Eq. (3) was used to calculate the trajectories of an ensemble of molecules. The connection between the Langevin equation and the convection-diffusion equation for concentration transport has been described in detail (Brenner and Edwards, 1993).

Solute dispersion is defined as the time rate of change in the second moments of molecule displacements,

$$\mathbf{D}(t) = \frac{1}{2} \frac{d\sigma^2}{dt}, \quad \sigma^2(t) = \frac{1}{n} \sum_{i=1}^n (\mathbf{d}_i - \langle \mathbf{d} \rangle)(\mathbf{d}_i - \langle \mathbf{d} \rangle)^T \quad (4)$$

where $\mathbf{d}_i$ is the displacement of molecule i from its initial position, $\langle \mathbf{d} \rangle$ is the ensemble average displacement at time t , and n is the ensemble size. In the case of no flow, $\langle \mathbf{d} \rangle = 0$ and $\mathbf{D}(t)$ is essentially the effective diffusion tensor. In the present simulations, the fluid pressure gradient is aligned with the z -axis and the mean displacement is nonzero. The diagonal components of $\mathbf{D}(t)$ correspond to dispersion along the Cartesian axes with $D_{zz} > D_{xx} \approx D_{yy}$. The time derivative $d\sigma^2/dt$ is approximated by $\sigma^2(t)/t$. This is not accurate where $\sigma^2(t)$ is nonlinear, but varies smoothly in time. A more accurate approximation to the derivative is subject to fluctuations about zero because $\sigma^2(t)$ is not necessarily strictly increasing over short time intervals, so statistical smoothing is required.

2.4.1. Unidirectional diffusion flux—The unidirectional diffusion flux J_0 is defined as the number of solute molecules moving in one direction across an interface per unit area per unit time by self-diffusion. An expression is deduced from Eq. (3) to approximate radial diffusion flux within the SPP,

$$J_0(r) = \frac{3}{2} \frac{D_0}{\Delta r} c(r) \quad (5)$$

where $J_0(r)$ is molar mass flow per unit area into the sphere $S(r)$ of radius r centered in the SPP, and $c(r)$ is the concentration of molecules in the thin spherical shell formed between $S(r)$ and $S(r + \Delta r)$. The quantity $3D_0/2\Delta r$ represents the average molecule velocity normal to $S(r)$ due to diffusive motion. It is derived as follows.

In the case of diffusive flux, the drift velocity term in Eq. (3) is ignored and a molecule (centroid) located at $r' \leq r + \Delta r$ in the shell travels with equal probability to any point on the surface of a sphere, B , of radius $s = \sqrt{6D_0\Delta t}$, with velocity magnitude $s/\Delta t$. Assume the shell is open to flow and $s < \Delta r$. Then the probability that the molecule centroid crosses $S(r)$ is the area of the spherical cap formed by the intersection of B and S , divided by the area of B , assuming $r \gg s$ and a planar approximation to $S(r)$. This probability is $2\pi sh/4\pi s^2$ where h is the height of the cap, noting that $h = 0$ where $r' - r > s$. Integrating this probability over the interval $[r, r + \Delta r]$ approximates the fraction of molecules in the shell that cross $S(r)$ in a time Δt .

$$\frac{s}{4\Delta r} = \frac{\int_r^{r+s} 2\pi s(r+s-r')dr'}{\int_r^{r+\Delta r} 4\pi s^2 dr'} \quad (6)$$

The product of Eq. (6) and the molecule velocity magnitude yields the probability-weighted average velocity $s^2/4r$ $t = 3D_0/2r$ given in Eq. (5). Eq. (5) thus approximates the unidirectional diffusion flux produced by the numerical method for a single time step in a shell open to flow. Note the molecule trajectories in Eq. (3) are not differentiable and a formal derivation of unidirectional flux in the limit of small t requires a different approach (Singer and Schuss, 2005).

3. Results

3.1. Accessible porosity

Accessible porosity, ϵ_A , is the void fraction that can be accessed by a probe of given radius. In the present work, it is calculated as

$$\epsilon_A = \frac{M_p}{M_{p,0}} \epsilon_p^s \quad (7)$$

where ϵ_p^s denotes the SPP intraparticle porosity based on the porous shell volume, M_p is intraparticle molar mass for molecules of radius r_{mol} , and $M_{p,0}$ is the intraparticle molar mass for the specific case $r_{\text{mol}} = 0.1375$ nm, the smallest molecule. The molar mass is initialized by placing molecules on a regular, finely-spaced lattice in the packed bed, excluding those which intersect a pore wall. The ratio can be calculated immediately after initialization, provided the initial placement doesn't include spaces large enough to accommodate a probe but inaccessible via diffusion. This possibility was evaluated by comparing values of M_p obtained under two different initial conditions: placing molecules in the intraparticle and interstitial regions versus placing molecules only in the interstitial region and allowing time for them to diffuse into the particle.

The first condition approximates a uniform concentration subject to steric exclusion by the pore surfaces and is termed the "static case." The second condition avoids introducing molecules into intraparticle locations which they could not naturally access via flow and diffusion and is termed the "dynamic case." Simulations using the dynamic case were allowed to run long enough to approach a steady state concentration and the results indicate that for $r_{\text{mol}} \leq 0.2r_{\text{sol}}$, molecules had access to all particle depths via transport. Therefore, the static case was used to calculate ϵ_A .

Fig. 2 plots ϵ_A versus dimensionless depth in the SPP shell for different values of r_{mol} . The values of $\epsilon_A(r)$ are calculated in radial shells of thickness Δr centered in the particle. The curve corresponding to $r_{\text{mol}} = 0.1375$ nm, the smallest molecule radius, is equivalent to $\epsilon_p^s(r)$.

As shown in this figure, the accessible porosity decreases with molecule size. The size

discrimination begins one sol layer below the outer hull and stays relatively constant into the shell until near the core, where the sol packing density is lower. The size-discrimination effect is the essential separation mechanism of SEC. As noted by Gu and coworkers (Li et al., 1998; Luo et al., 2013; Gu, 2015) using slightly different notation, the ratio of the average value of ϵ_A to ϵ_p^s is the SEC equilibrium constant K such that $0 \leq K \leq 1$ and

$$V_R = V_0 + KV_i \quad (8)$$

where V_R is the chromatographic retention volume, V_0 is the interstitial pore volume, and V_i is the intraparticle pore volume. K varies from an excluded zone ($K = 0$) when the solute is larger than the pore to a fully included zone ($K = 1$) when the solute is very much smaller than the pore. The average value of $K = \epsilon_A/\epsilon_p^s = M_p/M_{p,0}$ for each molecule size is plotted in Fig. 3, for the static and dynamic cases.

3.2. Intraparticle solute concentration

Where the size exclusion effect is significant, the intraparticle concentration tends to remain lower than the surrounding interstitial concentration, and a correlation between local concentration and the accessible pore volume fraction is found. Size exclusion effects become obvious where the molecule size is in the colloidal size range of $\geq 0.1 r_{\text{sol}}$. This will be shown below.

Fig. 4 shows concentration versus depth in the particle for the static and dynamic cases described earlier. Dimensionless concentration is denoted by $c(r)/\langle c \rangle$, where $c(r)$ is the molar concentration in a thin spherical shell at radius r , and $\langle c \rangle = M_T/(V_0 + V_i)$ is the average bed concentration, i.e. total solute mass divided by total pore volume. In both cases, there is an inverse relationship between molecule size and concentration. The concentration of larger molecules varies with the local porosity. Porosity drops to 50% below the first sol layer and concentration drops significantly in both cases. Porosity increases to 70% at the core and concentration increases in both cases. The interpretation is that average pore size varies with porosity, as would be expected in a random assembly of spheres. Accessible porosity versus depth is shown in Fig. 2.

The two cases differ in the interior region, below a depth of one sol diameter. In the dynamic case, the concentration of larger molecules gradually increases with depth while the static case concentration remains flat until close to the core. The concentration build-up in the dynamic case is interpreted as a convection effect associated with hindered transport around the core. The dynamic case is thought to more closely approximate a dynamic equilibrium.

The concentration near the core is elevated for two reasons. The first and most clear effect of size exclusion is a correlation between local porosity and concentration, and the local porosity is elevated near the core. A second, less clear effect is that concentration gradients may develop because motion is restricted. This would be analogous to the gradients that develop at a filter. The large core acts as a barrier, or filter, to the movement of solute.

Radial variations in concentration also develop even where size exclusion is not important. The concentration of the smallest molecule size is elevated above the interstitial average in the particle interior, which is a region of lower porosity. The effect appears regardless of the initial molecule distribution, with and without fluid flow, and develops rather quickly. Neither this effect – or the size exclusion effect – is significant for the next larger molecule size, which is larger by an order of magnitude.

3.2.1. Mixing of the interstitial fluid—When a solute is introduced into the packed bed, time is required to develop a steady state concentration distribution in the particles. The distribution develops more quickly if the interstitial fluid is well mixed. In the case of perfect mixing, concentration near the hull boundary is always equal to the interstitial average concentration (which decreases over time in the dynamic case as the particles gain solute mass). In simulation, the hull concentration generally remains below the interstitial average, even at short times (not shown). This indicates that mixing of the interstitial fluid is slow compared to diffusion into the particles. Fig. 4 also shows that for larger molecules, the interstitial average (square symbols) and hull concentrations remain elevated above (c) , which is evidence of the size exclusion effect.

3.2.2. Intraparticle mass fraction—The intraparticle solute mass fraction, M_p/M_T , is the fraction of total solute mass in the particles. The ideal mass fraction is the intraparticle pore volume divided by the total bed pore volume. However, the ideal is only achieved by small molecules because size exclusion reduces the actual mass fraction for larger molecules. Fig. 3 plots M_p/M_T versus solute molecule radius for the static and dynamic cases. Although the relationship is well fit by a linear function in this size range, theory and experiment suggest a more complex functional relationship as discussed in Section 3.3.2. The mass fractions in the dynamic case are elevated slightly above the static case. This reflects the larger concentration gradients that develop due to size exclusion in the dynamic simulations (cf Fig. 4).

3.3. Intraparticle solute flux

Intraparticle mass flux is driven by diffusion and convection. Flux into the particle hull is caused by solute movement from the interstitial region into the intraparticle region. Interstitial fluid flow wraps around the particles and the direction of flow tends to be tangent to the hull. Mass is transported into the hull by diffusive motion, e.g. a molecule jumps off the tangent streamline, and by convective motion, where the velocity has a component normal to the hull.

The relative importance of convection and diffusion can be characterized by the sol Peclet number (or scaled velocity magnitude), $Pe_{sol}(r) = |v(r)|d_{sol}/D_0$ where $|v(r)|$ is the mean pore velocity magnitude at radius r . Fig. 5 illustrates $Pe_{sol}(r)$ versus depth in the particle. For the smallest molecules, convection and diffusion are similar in magnitude at the hull but diffusion dominates convection below the first sol layer. For the largest molecule, convection dominates at the hull but the two contributions are similar below the first layer. Inside the hull, fluid velocity dissipates with depth. Mean fluid velocity decreases by two orders of magnitude from the particle hull to the core, with most of the decrease in the first sol layer.

However, convection continues to move solute in the general direction of the pressure gradient. The small bumps in Pe near the core boundary (vertical dashed red line) reflect slightly elevated fluid velocity near the core, caused by high porosity and larger pore spaces. This is similar to channeling along the wall of a packed column.

Intraparticle flux $J(r)$ is defined as the *unidirectional* mass flow per unit area into the sphere $S(r)$, where the area is taken as $\phi(r)4\pi r^2$, i.e. the area of S open to flow, with units of M/m^2s . The *superficial* flux, $\phi(r)J(r)$, is similarly defined but area is taken as $4\pi r^2$. Fig. 6 plots $J(r)$ versus dimensionless depth in the particle. $J(r)$ is inversely proportional to molecule size over the entire depth. The relative contributions of diffusion and convection to flux are more easily seen in Fig. 7, which replots $J(r)$ in the dimensionless form, $J(r)/J_0(r)$, where $J_0(r)$ is the diffusive flux predicted in (Eq. 5). In regions where $J(r)$ results primarily from molecular diffusion, it is expected that $J(r)/J_0(r) \approx 1$. At depths greater than a sol diameter, the curves for different molecule sizes do collapse to a great extent, consistent with diffusive flux rates. But in the first sol layer, $J(r)/J_0(r) > 1$ for some sizes. Although the three smallest sizes display an increasing trend consistent with local Peclet number, the largest molecule size shows no significant convection effect near the hull.

A similar relationship between molecule size and non-dimensional flux near the hull was found in a body-centered cubic (BCC) packing of SPP particles. A larger molecule size, $0.4r_{sol}$, also showed no significant effect of convection near the hull. These results indicate that hull flux is diffusion-limited in the large λ regime, e.g. $\lambda > 0.1$, in spite of the fact that larger molecules are characterized by higher Peclet numbers. Evidently their tangent momentum around the hull is less easily or less frequently translated into normal momentum through the hull.

3.3.1. Intraparticle effective diffusion—The intraparticle effective diffusion coefficient, $D_{SPP}(r)$, is the calculated rate at which $\langle c \rangle$ must diffuse to produce the superficial flux $\phi(r)J(r)$. $D_{SPP}(r)$ is calculated using the diffusive flux model in Eq. (5) by substituting $\langle c \rangle$ for $c(r)$ and $\phi(r)J(r)$ for $J(r)$ and rearranging terms to obtain

$$D_{SPP}(r) = \frac{2}{3} \frac{\Delta r \phi(r) J(r)}{\langle c \rangle} \quad (9)$$

The dimensions remain those of flux, $M=m^2s$. ϕ incorporates the effect of porous media occupying part of the space, so in the absence of convection, $D_{SPP} \leq D_0$.

$D_{SPP}=D_0$ versus depth in the particle is shown in Fig. 8. Larger molecules generally have lower dimensionless effective diffusion rates. Exceptions occur near the hull, where $D_{SPP} > D_0$ for two sizes, and this reflects the competition between convection and size exclusion effects discussed in the previous section.

3.3.2. Effective diffusion vs accessible porosity—Effective diffusion is often predicted by correlations of the general form

$$D_{\text{eff}} = \frac{\epsilon D_0}{\tau} \quad (10)$$

where τ is the tortuosity (Guiochon et al., 2006; Carta and Jungbauer, 2010). This was originally derived assuming a small molecule relative to the pore size. In the present work, intraparticle effective diffusion is predicted by a correlation of the form

$$D_{\text{SPP}} \approx \epsilon_A D_0 \quad (11)$$

The correlation of D_{SPP} and ϵ_A is shown in Fig. 9.

The correlation in (Eq. 11) can be derived from Eqs. (5) and (9) so that it should hold in the present work is unsurprising. However, the same correlation is evident in a separate work using a different geometry, a silica monolith, and different methods for calculating effective diffusion and accessible porosity (Hlushkou et al., 2017). This coincidence recalls Renkin (1954), who defined the dimensionless accessible area, A/A_0 , and studied its correlation with experimentally measured diffusion. He presented two closely related equations modeling A/A_0 for the cases of hindered diffusion ((Eq. 11)) and ultrafiltration (Eq. (19)). Both have the same expression for pore friction combined with a term describing pore entrance effects. In (Eq. 11) this term simply describes the effective pore area while in Eq. (19) the term captures the convection effect, that molecules entering the pore through the reduced effective area are traveling at higher speeds based on a Poiseuille distribution. Since convection plays a role in the present work, Renkin's Eq. (19) is the more appropriate comparison. Renkin's equations are plotted in Fig. 9 as $\epsilon_p^s A/A_0$ versus λ , where $\epsilon_p^s \approx 0.58$ is the SPP intraparticle porosity and, coincidentally, the monolith porosity in Hlushkou et al. (2017).

3.4. First passage time

A molecule's internal age is the elapsed time since entering a particle and is denoted as I_p . The first passage time, $I_p^f(r)$, is the average age when molecules first reach depth r in the particle. Larger molecules have longer first passage times because they diffuse more slowly. Since diffusion is the primary but not the only mechanism for transport in a particle, a natural time unit for passage is d_{sol}^2/D_0 , or the time to diffuse one sol diameter. Table 4 gives this diffusion time for different molecule sizes. The other terms in this table are defined below in Sections 3.5.1 and 3.6.2.

Fig. 10 plots the dimensionless mean first passage time, $I_p^f(r)D_0/d_{\text{sol}}^2$, versus the dimensionless depth in the particle, $(r_h - r)/d_{\text{sol}}$, for the SPP random pack. The curves for different molecule sizes collapse almost entirely when plotted in this dimensionless form. Differences between molecule sizes are therefore explained almost completely by the

diffusion coefficient. It does not imply that convection is unimportant, only that its effect on first passage time appears independent of molecule size.

3.5. Age versus depth

Age reflects transport time in the particle, so it is influenced by both convection and diffusion. For a given flow rate, the relative magnitude of diffusive and convective contributions depends on the molecule size and diffusion coefficient. Fig. 5 shows that for small molecules, the two contributions are similar in magnitude at the hull but diffusion dominates convection below the first sol layer. For the largest molecule, convection dominates at the hull but the two contributions are similar below the first layer. Based on this analysis, a “quasi-diffusive” time scale – similar diffusive and convective contributions – is expected to prevail generally for all molecule sizes, except for larger molecules at shallow depths, where convection effects should be evident.

The internal age, $I_p(r)$, is the mean age of molecules located at a given depth, r , at some instant. Fig. 11 plots the dimensionless mean age, $I_p(r)D_0/d_{\text{sol}}^2$, versus the dimensionless depth in the particle, $(r_h - r)/d_{\text{sol}}$, for the SPP random pack. Since age is made dimensionless by diffusion time, the curves should collapse if differences between them are explained by the diffusion rate. The collapse is not complete in the first sol layer where $(r_h - r)/d_{\text{sol}} < 1$, which shows an inverse relation between dimensionless age and molecule size. This is interpreted as the convection effects predicted for larger molecules at shallow depths. Fluid velocities near the hull are on the same order as the mean bed velocity. For larger molecules, that velocity exceeds the diffusive contribution by two orders of magnitude. This does not imply greater flux of large molecules because hindrance increases with size, but reflects the higher Peclet numbers experienced by large molecules near the hull (cf Fig. 5 and Section 3.3). Near the hull, convection speeds the motion of molecules into or out of the particle, relative to diffusion.

Below the first sol layer, a quasi-diffusive time scale is expected because convection is on the same order as diffusion for the largest molecules. Additionally, there is an expectation that diffusion paths around the core will be longer for larger molecules, increasing their diffusion time and dimensionless average age at greater depths. A weak correlation between age and size is evident among the three smallest molecules in the deeper range $(r_h - r)/d_{\text{sol}} > 1$, which is consistent with the expectation, but the largest molecule has lower dimensionless age compared to the other sizes, which is contrary to the expectation and correlation (Fig. 11). This result is interpreted as an artifact as explained below.

3.5.1. Convergence of the age distribution—The age distribution requires some time to approach a steady state and larger, slower molecules require more time to develop a steady distribution. Shallow depths are populated earlier and have lower average age, so the age distributions tend to converge sooner near the hull. Convergence can be judged from the change in mean age versus time. An inspection of the simulation histories (not shown) indicates the mean age of the largest molecules is not fully converged at depths greater than one sol layer. The same is noted for the second-largest molecule, although to a lesser degree and at greater depths. This implies the mean age is still increasing and is therefore

underestimated at greater depths in the particle. Table 4 shows the simulation time in physical units and in dimensionless form, scaled by the time to diffuse a distance r_{sol} . Note small molecules have a shorter physical simulation time and longer dimensionless time than larger molecules. As a practical matter, the simulation time should exceed the maximum molecule age by a significant factor to assure convergence.

3.6. Age distribution

The molecule internal age distribution, $I_p(t)$, is the age density function for molecules in particles, at a given instant. Some time is required for the age distribution to develop. Gradually, the numbers entering and leaving the particles achieve a balance and the age distribution reaches a steady state, where the number of molecules of each age is stable. But the age distribution is always dominated by the number of “young” molecules, because flux is greatest near the particle hull where age tends to be small.

The probability that a molecule in a particle has an age t is given by $I_p(t)dt$, where $I_p(t)$ is the age density function, with units of inverse time. The cumulative age distribution, $\int_0^t I_p(t')dt'$, gives the probability that a molecule has age less than t . Fig. 12 plots the age cumulative probability distribution versus the dimensionless time, tD_0/d_{sol}^2 , where t is the variable quantity and D_0/d_{sol}^2 is a constant for each molecule size curve. A unit step on the x-axis is the time to diffuse an average distance of one sol diameter. Note this is just a different view of the same data shown in Fig. 11, where molecules of different ages were averaged by depth in the particle. Again, if diffusion rates explain differences in age, the curves should collapse.

An inverse relation between age and molecule size is seen in Fig. 12 for dimensionless time $tD_0/d_{\text{sol}}^2 < 5$. This reflects the differential effects of convection, as discussed in Section 3.5. Molecules closer to the hull have lower ages and larger ones are more affected by convection. The comments on convergence in Section 3.5 also apply to this data. The high end of the age range is not completely developed for the larger molecules. The low end of the age range is not thought to be significantly affected by this issue. The effect is to elevate the fraction of large molecules in the range $5 < tD_0/d_{\text{sol}}^2 < 10$. It is expected that with additional simulation time, the fraction of large molecules older than 10 would increase and the curves would cross over in that range.

3.6.1. Exit age distribution—The age of a molecule on exit from the particle is denoted by E_p , the exit age. Over a given period, a molecule makes many visits of different duration to various particles. For all molecule sizes, 99% of the visits are less than one dimensionless time unit (the time to diffuse the sol diameter). This can be interpreted as the effect of Brownian motion near the particle hulls. Each molecular transit across the hull is counted as a visit, and the exit age is often much shorter than a dimensionless time unit.

The probability of exit age t is given by $E_p(t)dt$, where $E_p(t)$ is the exit age density function, with units of inverse time. Note the exit age and internal age distributions have a special relationship at steady state, given by $E_p(t) = -(d/dt)I_p(t)$ where β is the mean residence time

of a reactor, given by the ratio of bed volume to volumetric flow rate (Nauman, 2008). The exit age cumulative probability distribution, $\int_0^t E_p(t')dt'$, gives the probability that a visit is less than or equal to t .

Fig. 13 plots the cumulative exit age distribution versus dimensionless diffusion time. The curves do not collapse completely and show an inverse relation between visit time and molecule size. This indicates the larger molecules tend to have shorter exit ages than would otherwise be predicted by their diffusion rate. Because the exit age distribution is dominated by short visits, its behavior is generally similar to the early-age range of the age distribution (Fig. 11), where convection effects become important for larger molecules.

3.6.2. Ratio of time in particles to time in bed—If the internal age distribution is at steady state, the number of molecules in particles is invariant, and it follows that the fraction of time spent by molecules in particles is simply the ratio of the intraparticle population to the total population in the packed bed, or the ratio of the two molar quantities. Table 4 gives this ratio, along with the estimated cumulative particle visit time (cf Fig. 3). The largest molecules spent an average of 28% of the time in particles, compared to 39% spent by the smallest. Note the cumulative visit times are calculated from the internal age distribution at the end of the simulation ($t_{\max}$) under the assumption the distribution is at steady state. Total bed time is the number of molecules multiplied by $t_{\max}$.

3.7. Dispersion and effective diffusion

Dispersion is generally greater in an SPP packed bed than a comparable bed of solid spheres, because the porous particles tend to hold up the solute molecules. The exact conditions under which this is true depend on the ratio of convection and diffusion and the details of the comparison. In the present case, the two packed beds have the same particle arrangement, the same average pore velocity and the solid sphere diameter is equal to the SPP hull. But as a consequence, the SPP bed has more pore volume, a higher pressure gradient, and a higher interstitial average velocity as shown in Table 2.

Fig. 14 plots the dimensionless dispersion coefficient versus dimensionless diffusion time tD_0/r_{sol}^2 for the four molecule sizes. Note in this case time is made dimensionless by the time to diffuse over a hull radius, which is a relevant scale in both the solid-sphere and SPP packed beds. Although convection is significant, the diffusion time scale is important in understanding differences in development time among the different molecule sizes.

The dispersion coefficient correlates with molecule size in Fig. 14 because the larger molecules have smaller molecular diffusion coefficients and a correspondingly larger convective contribution to molecule displacements. The hull Peclet number, $Pe_h = \bar{v}r_h/D_0$, is two orders of magnitude greater for the largest molecule size compared to the smallest.

The curves corresponding to the solid-sphere packed beds, shown in dashed line, track closely with the SPP beds but diverge after a period of time for the larger molecules. Solute is introduced initially to the interstitial region and gradually enters the porous particles, eventually causing the dispersion coefficients of the SPP and solid-sphere beds to diverge.

Divergence does not appear for the smallest molecule, which may be explained by the relatively low Peclet number. For the next largest molecule size, $r_{sol} = 1.438$ nm, the curves are flattening their approach to the asymptotic value, and it may be surmised that the eventual difference between the SPP and solid-sphere coefficients will be less than an order of magnitude. The situation is quite different for the two largest molecule sizes, where the solid-sphere curves appear to be flattening out while the SPP curves are increasing rapidly.

As a point of reference, Fig. 14 also shows the effective diffusion coefficients for the case of no flow in the solid-sphere packed bed. The curves corresponding to the four different molecule sizes are completely collapsed, indicating that differences in the coefficients are completely explained by the molecular diffusion rates. This is expected because even the largest molecule size is very small in relation to the sphere diameter ($r_{mol}/r_h \approx 0.005$) and, hence, the interstitial pore size. The square symbols denote the terminal time value for the respective curves. The curves appear to be approaching an asymptotic value of $D_{eff} \approx 0.7$.

4. Conclusions

The size exclusion effect became significant in this study when the molecule diameter was increased from $0.025r_{sol}$ to $0.1r_{sol}$. The effect was to reduce the intraparticle solute mass fraction below that expected based on particle void fraction. A linear relationship between molecule size and intraparticle mass fraction was noted. Where the size exclusion effect is significant, intraparticle concentration correlates with radial variations in the local intraparticle void fraction, which are greater near the SPP particle hull and core. Mixing of the interstitial fluid appears slow compared to diffusion into the particles based on the finding that near-hull concentration remained below the interstitial average concentration over time.

Molar flux into the SPP particles depends on convection and diffusion. Convection is significant at the SPP particle hull but decreases sharply with depth. For small sol Reynolds numbers, convection effects are not generally significant in the particle interior and the flux is well predicted by the molecular diffusion rate. Near the hull, convection dominates for larger molecules with small diffusion rates, but is comparable to diffusion for smaller molecules. Where convection dominates, molar flux is somewhat greater than predicted by diffusion up to a certain size, where other effects constrain flux to diffusive rates. The relationship between size exclusion, flow rate, and pore geometry is complex and some insight may be gained from the study of more idealized geometries. One of the authors (MRS) is currently investigating size selectivity in perpendicular networks of cylindrical pores where it appears that even in simple geometries, pore entrance effects show a large dependence on solute size and diffusion coefficient.

In general, the intraparticle age distribution is dominated by “young” molecules near the hull, where molar flux is greatest, and the cumulative intraparticle residence time of a typical molecule is characterized by multiple short visits to the first sol layer of SPP particles. Solute molecules migrate toward the SPP core from all directions. Although a pressure gradient exists throughout the packed bed, the time scale for first passage to a given depth is well predicted by diffusion. But intraparticle residence time is not as well predicted. Where

convection effects are significant – for larger molecules near the hull – the expected age is generally lower than predicted by the diffusion rate. At a steady-state concentration, the ratio of intraparticle residence time to total time in the packed bed is given by the intraparticle mass fraction.

The simulations showed that the transport of solute into and out of the SPP shell was aided by convection through the outermost surface layer of sol particles, while deeper transport was essentially diffusive and limited by the accessible pore volume within the particle; the Peclet number based on sol radius approached unity only for the largest molecules. The low Reynolds number associated with intraparticle flows permits some generalization of this physical picture to higher interstitial flow rates. Convection brings solute molecules to the particle interior, but for convection to dominate interior flow, the sol size and/or pressure gradient must be increased significantly. Otherwise, mass transport is ultimately limited by diffusion once “inside” the particle. Absent such major increases in flow and pore size, separation media that more effectively convert tangent flow into hull flux can be expected to deliver better chromatographic efficiency at moderately higher flow rates. In any case, the results suggest that if porous shells used in SPPs are made thinner and more porous, the chromatographic efficiency in analytical-scale chromatography can be maximized. However, practical considerations limit this because thinner and more open shells reduce surface area and hence retention in the particle when retention is driven by surface association with a chemically-bonded surface phase. These results suggest that so-called “perfusion chromatography,” (Lloyd and Warner, 1990; Afeyan et al., 1991; Rodrigues et al., 1993; Frey et al., 1993; Rodrigues, 1997; de Neuville et al., 2014; Wu et al., 2015) where mass transport in the porous layers is convectively driven through porous particle assemblies due to significant fluid velocity in the porous shell, will succeed for only the largest pore diameters and thinnest shells. This may be accomplished with a loss of surface area and possibly mechanical stability as a compromise between chromatographic efficiency and retention range. Such optimization, while worthwhile, may be the ultimate limitation of using convection for efficiency enhancement in large-pore large-molecule chromatography.

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Symbols appearing in Figures

$\langle c \rangle, c(r)$	Molar concentrations, bed average and intraparticle average at radial position r (M/m ³)
D_0	Molecular self-diffusion coefficient (m ² /s)
D_{eff}	Effective diffusion coefficient for bed (m ² /s)

$D_{\text{SPP}}(r)$	Intraparticle effective diffusion coefficient, average at radial position r (m^2/s)
D_{zz}	Longitudinal dispersion coefficient for bed (m^2/s)
d_{sol}	Sol diameter (m)
E_p	Exit age of molecule leaving particle (s)
$I_p; I_p(r)$	Molecule internal age in particle and average age at radial position r (s)
$I_p^f(r)$	Average internal age at time of first passage to radial position r (s)
$J(r)$	Unidirectional intraparticle flux at radial position r ($\text{M}/\text{m}^2 \text{ s}$)
$J_0(r)$	Unidirectional intraparticle diffusion flux ($\text{M}/\text{m}^2 \text{ s}$)
K	Size exclusion constant (dimensionless)
M_p	Intraparticle molar mass (M)
$M_{p;0}$	Intraparticle molar mass for water (M)
M_T	Total molar mass for bed (M)
Pe_{sol}	Peclet number based on sol diameter d_{sol} (dimensionless)
r_h	Hull radius (m)
r_{mol}	Molecule radius (m)
r_{sol}	Sol radius (m)
$\epsilon_p^s(r)$	Intraparticle porosity at radial position r (dimensionless)
$\epsilon_A(r)$	Accessible porosity at radial position r (dimensionless)

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HIGHLIGHTS

- Size exclusion significant when molecule-sol size ratio increased from 0.025 to 0.1.
- Size exclusion effects include correlation between concentration and void fraction.
- Convection dominates near the hull for larger molecules with small diffusion rates.
- Flux well predicted by molecular diffusion rate deeper within SPP.
- Time scale for molecular first passage to given depth well predicted by diffusion.
- Intraparticle age not as well predicted by diffusion.
- Intraparticle age distribution dominated by young molecules near the hull.
- Cumulative residence time characterized by multiple short visits to first sol layer.

Fig. 1.

Random packing of 125 SPP in a cubic bounding box with periodic boundaries. Core particles are shown in translucent orange. Outer sol layers shown in pink-gray and inner sol layers in primary colors. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

Fig. 2. Accessible porosity versus dimensionless depth in particle for different molecule sizes. Note, $\epsilon_A = \epsilon_p^s$ for $r_{mol} = 0.137$ nm.

Fig. 3. Intraparticle mass fraction (M_p/M_T) and SEC equilibrium constant (K) versus dimensionless molecule size. Static and dynamic cases are denoted by squares and circles, respectively. Dashed lines are linear least squares fits of the data.

Fig. 4. Dimensionless concentration versus dimensionless depth for different molecule sizes. A: static case, B: dynamic case. Square symbols denote the interstitial average concentration.

Fig. 5. Sol particle Peclet number versus dimensionless depth in the SPP for different molecule sizes.

Fig. 6.
Unidirectional molar flux versus dimensionless depth in particle for different molecule sizes.

Fig. 7.
Dimensionless molar flux versus dimensionless depth in particle for different molecule radii.

Fig. 8.
Dimensionless effective diffusion versus dimensionless depth in particle for different molecule sizes.

Fig. 9.

Correlation between effective diffusion and accessible porosity vs dimensionless probe size.

D_{eff} is the effective diffusion coefficient in a silica monolith from Hlushkou et al. (2017).

D_{SPP} is intraparticle effective diffusion in the present work.

Fig. 10.
Dimensionless mean first passage time vs dimensionless depth in particle for different molecule sizes.

Fig. 11.
Dimensionless mean age versus dimensionless depth in particle for different molecule sizes.

Fig. 12.
Internal age cumulative probability distributions for different molecule sizes.

Fig. 13.
Exit age cumulative probability distributions for different molecule sizes.

Fig. 14.

Dimensionless longitudinal bed dispersion vs dimensionless time for different molecule sizes. Solid curves denote the SPP packed bed and dashed curves denote the solid-sphere packed bed. Square symbols on collapsed curves denote the terminal simulation times for no-flow simulations in the solid-sphere packing. Numeric values denote the hull Peclet number.

Table 1

Packed bed characteristics, including simulation box dimension, L , number of particles, N , total bed porosity, ϵ_T , and interstitial and intraparticle void volume as fractions of bed volume, ϵ and ϵ'_p , respectively. The last column is the intraparticle void volume as a fraction of the shell volume, ϵ_p^s .

Packing	L (μm)	N	ϵ_T	ϵ	ϵ'_p	ϵ_p^s
random SPP	19.89	125	0.550	0.341	0.208	0.579
random solid sphere	20.08	125	0.360	0.360	0	0
BCC SPP	4.896	2	0.517	0.294	0.223	0.579
BCC solid sphere	4.959	2	0.320	0.320	0	0

Table 2

Bed velocity, q_z , pressure gradient, dp/dz , permeability from Darcy's equation, k , and dimensionless pore velocity in the direction of the pressure gradient for simulated solid and porous particle packed beds. All cases are simulated at $Re_{sol} = 10^{-3}$ and the average pore velocity in the direction of the pressure gradient is $\bar{v}_z = 8.694 \times 10^{-3}$ m/s. The average pore velocity within the porous particles and in the interstitial region is made dimensionless by dividing by $\bar{v}_z$.

Packing	q_z (m/s)	dp/dz (kg/m ² s ²)	k (m ²)	Dimensionless pore velocity	
				Intraparticle	Interstitial
Random SPP	4.75×10^{-3}	3.78×10^8	1.26×10^{-14}	0.067	1.57
Random sphere	3.13×10^{-3}	2.62×10^8	1.20×10^{-14}	0	1.00

Table 3

Molecular tracers and size relationship to pore radius and sol radius.

r_{mol} (nm)	λ	$r_{\text{mol}}/r_{\text{sol}}$	D_{θ} (m ² /s)	Similar to
0.1375	0.00275	0.00239	1.568×10^{-9}	Water
1.438	0.0288	0.025	1.499×10^{-10}	Small polymer
5.750	0.115	0.1	3.748×10^{-11}	Colloidal particle
11.50	0.23	0.2	1.874×10^{-11}	Colloidal particle

Table 4

Molecule radius, diffusion time, physical and dimensionless simulation time, cumulative visit time, total bed time, and their ratio for different molecule sizes.

r_{mol} (nm)	d_{sol}^2/D_0 (s)	t_{max} (s)	$t_{\text{max}}D_0/r_{\text{sol}}^2$	Visit time (s)	Bed time (s)	Ratio
0.1375	8.437×10^{-6}	0.0015	177.8	3.812×10^4	9.781×10^4	0.39
1.438	8.820×10^{-5}	0.0100	113.4	2.471×10^5	6.498×10^5	0.38
5.750	3.528×10^{-4}	0.0100	28.34	2.235×10^5	6.425×10^5	0.35
11.50	7.056×10^{-4}	0.0100	14.17	1.790×10^5	6.327×10^5	0.28