General Rules for the Optimal External Porosity of LC Supports

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We present a series of numerically calculated plate height and flow resistance data obtained for an idealized chromatographic support mimic with variable bed porosity (0.3 ≤ ϵ ≤ 0.9), yielding a unique insight into how the main chromatographic performance parameters can be expected to vary with the external bed porosity, unbiased by any differences in molecular diffusivity or retention factor. The influence of pore heterogeneity effects is considered as well. It is found that the product \( h_{\text{min}\text{opt}} \) depends only very weakly on ϵ and on the degree of pore heterogeneity. It is also found that the minimal separation impedance \( E_{\text{min}} \) decreases monotonically with ϵ. This shows that the minimal plate height increase that can be expected for large porosity systems is always more than compensated by their reduced flow resistance, in agreement with the current observations in real silica monolith columns. Using the computed plate height data in an optimization analysis, it is found that large porosity supports can always potentially yield shorter analysis times or larger plate numbers than small porosity supports but need submicrometer feature sizes to actually achieve this. Assuming a lower limit on the producible or useable structural feature sizes, it is found that small \( N \) separations can best be performed with a small porosity packing, whereas large \( N \) separations require a large porosity packing if the column length (L) is left free. A plot yielding \( \epsilon_{\text{opt}} \) as a function of the required plate number has been established, showing that roughly \( \epsilon_{\text{opt}} \sim \log(N) \) in both the ordered and the disordered support cases. It is also shown that the maximal increase in peak capacity ever to be expected from the use of high porosity supports is a factor of 2 (if the mobile-phase viscosity can be kept constant), potentially to be increased by a factor of 1.5 by increasing the homogeneity of the packing.

The present study fits in the recent trend to pursue improved chromatographic performances by switching to alternative support designs.1-2 With the introduction of monolithic columns3-8 and the first prudent attempts to employ the micromachining methods from the microelectronics industry to manufacture homogeneously etched chromatographic media,9-10 the external porosity of LC supports is no longer fixed to the typical ϵ = 0.35–0.4 value of the packed bed of spheres, but has become a more or less freely selectable optimization parameter. Unfortunately, there currently is little or no theoretical ground to select the optimal porosity as a function of the required separation efficiency. From the (relatively scarce) experimental data, it is known that the separation impedance decreases with increasing porosity,8,10,11 but there is no clear overall picture yet of how these small separation impedances translate into real column and skeleton dimensions as a function of the required number of theoretical plates. It is also not very clear whether one should continue to make efforts in the direction of very open pore structures or either in the direction of more compact structures but with an increased pore uniformity.

Apart from their scarceness, another problem with the experimental data is that the porosity effect is always partly masked by differences in column heterogeneity, by differences in retention factor \( k' \), and by differences in mobile and stationary zone diffusivity. To obtain a general insight into the effect of the bed porosity on the separation efficiency and the separation speed of HPLC columns, unbiased by any of the above-mentioned experimental problems, we have set up a computational study to calculate the band broadening and the separation impedance in a series of simplified, perfectly ordered 2-D column mimics with a variable external porosity ϵ (going from ϵ = 0.3 to ϵ = 0.9), but with a similar degree of isotropicity and pore homogeneity. The column mimics are based on 2-D arrays of circular solid-phase zones (diameter \( d_s \)) with an equilateral triangular arrangement. Each solid zone can either be considered as one of the particles in a particulate packing, as the cross section of a monolithic skeleton branch, or as a porous pillar in a 2-D etched column.12 For each considered porosity, it is ensured that the internal porosity \( \epsilon_{\text{int}} \), the phase retention factor \( (k' = 1.25) \), and the mobile and stationary zone diffusivities \( (D_m \) and \( D_s) \) remain constant. It

should be noted that the condition of a constant $k'$ implies that the different porosity systems can be compared for the same resolution by simply keeping the number of plates constant, as can be seen from the following, well-established resolution equation:

$$R_s = \frac{\sqrt{N}}{4} \frac{(\alpha - 1)}{\alpha} \frac{k'}{(1 + k')} \quad (1)$$

The present paper consists of two parts. In the first part, the relation between the external bed porosity and the band broadening and the flow resistance is determined. In the second part, these data are used to determine the optimal bed porosity for a number of important optimization criteria (maximal number of plates, minimal separation time, etc.). Obviously, a number of 3-D effects will be missed by making the 2-D approximation, but the main purpose of the computed ordered array data is to provide a general insight and to feed a set of consistent data to the optimization procedure. This optimization part is furthermore written in a general way, such that the qualitative conclusions do not stand or fall with the practical relevance of the 2-D array data. Most of the employed optimization procedures have already been established many years ago, among others, by Giddings and Knox. They showed that the most compact form of writing is established many years ago, among others, by Giddings and Knox. They have, for example, been used to determine the optimal particle diameter for packed-bed HPLC, to compare the performances of packed-bed and open-tubular systems, and to optimize the diameter of capillary LC columns. The same equations and approaches can now be revisited for the selection of the optimal bed porosity of LC columns. In the first place, the optimization will be based on the computed ordered array data, yielding the ultimate performance limits ever to be expected from packed-bed or monolithic column HPLC. The main aim of investigating these idealized structures is to gain a theoretical insight into how the external porosity influences the performance of particulate LC supports, independently of any differences in stationary and mobile zone diffusivities and any differences in the degree of structural heterogeneity. With real columns, the latter factors always tend to bias the comparison between columns with a different porosity. The data on the idealized 2-D structures is, however, also useful in itself. Apart from Regnier group, there is now also a group in Denmark working on the development of regular pillar columns.

In addition, the optimization will also be repeated on a series of band-broadening data obtained by starting from the ordered array data and adding a fixed increment to the $A$-term value, so as to approximate the band broadening in real chromatographic systems, which is known to be strongly influenced by the flow-through pore heterogeneity.


**CONSIDERED OPTIMIZATION PROBLEMS**

The two main goals of the current efforts to create new and better chromatographic systems are the minimization of $t_R$ for a given $N$ and the maximization of $N$ for a given $t_R$. The general optimization approach to solve these problems has already been established many years ago, among others, by Giddings and Knox. They showed that the most compact form of writing is obtained by switching to dimensionless variables. Doing so, the analysis time $t_R$ and the column length $L$ can be written as

$$t_R = \frac{L}{u_0 (1 + k')} = \frac{Nd_{ref}^2}{D_{in}} \frac{h}{\nu} \frac{(1 + k')}{(1 + k)} \quad (2)$$

and

$$L = Nh d_{ref} \quad (3)$$

Writing Darcy’s law in terms of the column permeability $K_v$,

$$K_v = u_0 \eta L / \Delta \phi$$

it is customary to define a dimensionless flow resistance, using

$$\phi = d_{ref}^2 / K_v \quad (4b)$$

Together with a generalized Knox equation, describing the band broadening behavior,

$$h = A \nu^\phi + B / \nu + C \nu \quad (5)$$

these equations form a closed set of equations determining $t_R$, $L$, and $N_{max}$ for every possible value of $\Delta \phi$, $D_{in}$, $\eta$, and $d_{ref}$.

It should be noted that detection-related optimization criteria, such as mass loadability, dynamic range, and detection limit, are not included in the current optimization study because these quantities are sample-specific and cannot as easily be compiled into a few simple equations such as $t_R$ and $L$. In general, it should, however, be remarked that these detection-related issues are to a large extent determined by the phase ratio. As a general warning, it should be noted that, since the phase ratio is proportional to $(1 - \epsilon)/\epsilon$, it decreases ~20-fold when going from $\epsilon = 0.3$ to $\epsilon = 0.9$. This implies that if a large porosity system is to achieve the same retention factor $k'$ as a low porosity system, a much lesser solvent will have to be used. For samples with a large dynamic range, this will quite rapidly lead to solubility problems and to an overloading of the stationary phase. Any place where the below optimization exercises point at the use of high porosity systems, this drawback should be kept in mind.

The remainder of this section is intended for the reader interested in the specifics and physical interpretation of the optimization procedures.

(23) Vervoort, N.; Gail, P.; Baron, G. V.; Desmet, G. J. Chromatogr., A 2004, 1030, 177–186.
To keep the established optimization and constraint equations as general as possible, they have been written in terms of an undefined reference distance \(d_{ref}\), leaving the possibility of filling in any characteristic distance. For reasons of simplicity, we only consider cases where the column length is left free.

The free column length problem obviously is the problem with the largest degree of freedom and hence yields the ultimate performance limit of chromatographic systems. Mathematically, it can be expressed by eliminating \(L\) from the performance equations given in eqs 4a,b and in eqs 2 and 3, yielding\(^{26}\)

\[
vh = \Delta p d_{ref}^2 / \phi D_m n = \pi \tag{6}
\]

From its definition, \(\pi\) can be considered as a dimensionless pressure,\(^{14,26}\) as is discussed further under 2. Fixed \(d_{ref}\). Combining eq 6 with the reduced plate height expression (eq 5), a solvable set of two equations with two variables (\(h\) and \(n\)) is obtained. Due to the nonlinear nature of eq 5, the solution, however, has to be determined numerically. In the present study, this has been carried out using a self-written Visual FORTRAN numerical routine, based on the successive bisection method.\(^{27}\) A closer inspection of the combination of eqs 5 and 6 reveals that a positive solution for the reduced velocity \(v\) can only be obtained if

\[
\pi > B
\tag{7}
\]

This constraint obviously needs to be taken into account when writing the program. Rewriting eq 7 with the definition of \(\pi\) given in eq 6, it is found that

\[
d_{ref}^2 > \phi D_m n NB / \Delta p
\tag{8}
\]

The constraint in eq 8 expresses that a given number of plates \(N\) can only be achieved with a packing with a sufficiently large reference distance \(d_{ref}\). As was noted initially by Giddings,\(^{14}\) this limiting value can be directly calculated from eq 8 since all the variables on the right-hand side are known.

1. Free \(d_{ref}\). This obviously is the most simple optimization problem. Since \(d_{ref}\) is free, eq 6 can be used to replace \(d_{ref}\) in eq 2 and to eliminate it from the problem. This yields

\[
t_R = (N^2 \eta / \Delta p) h^2 \phi (1 + k')
\tag{9}
\]

Equation 9 immediately shows that, for a given \(\epsilon\), \(t_R\) is minimal if and only if \(h = h_{min}\) (\(\phi\) is constant for a given \(\epsilon\)). Since \(h_{min}\) is achieved when \(v = v_{opt}\), this implies that the absolute minimal analysis time is obtained in a column with a \(d_{ref}\) selected such that it can operate at the optimal velocity \(v_{opt}\) while being exactly long enough to yield the desired number of plates without exceeding the pressure drop limit, a rule initially established by Knox and Saleem.\(^{15}\) Since \(h_{min}\) and \(v_{opt}\) are independent of the value of \(d_{ref}\) they can now be introduced as constants into eq 6 to yield an expression for the optimal \(d_{ref}\):

\[
d_{ref, opt}^2 = (\phi D_m n / \Delta p) h_{min} v_{opt}
\tag{10}
\]

Since \(h_{min}\) and \(v_{opt}\) are also independent of \(N\) (and \(L\)), eq 10 also directly shows that for every plate number \(N\) a different \(d_{ref, opt}\) exists. In other words, if the Knox and Saleem condition is to be satisfied, a column with a different solid size is needed for each different value of \(N\). Consequently, these columns would also all have a different length.

From eq 10, it is also straightforward to define \(t_{opt}\) as

\[
t_{opt} = v_{opt} h_{min} = \Delta p d_{ref, opt}^2 / \phi D_m n N
\tag{11}
\]

With this definition, and the fact that \(\pi\) can be considered as a dimensionless pressure (cf. eq 6), the condition of \(\pi \gg \pi_{opt}\) can be considered as an indication of the availability of a large amount of excess pressure allowing operation of the system at \(v \gg v_{opt}\), which is, for a given \(d_{ref}\), always the condition yielding the shortest possible separation time.\(^{28}\) If \(\pi\) is very large, the excess pressure can of course also be used to switch to a packing with smaller \(d_{ref}\), bringing \(\pi\) closer to \(\pi_{opt}\). Whether \(\pi\) is large because \(\Delta p\) is large in itself, because \(d_{ref}\) is large, or because \(N\) is small does not matter. The condition of \(\pi < \pi_{opt}\) on the other hand implies that the available inlet pressure is so small that the system needs to be operated below \(v_{opt}\) which strongly increases the required analysis time.

Under the condition of \(h = h_{min}\) it is easy to see from eq 9 and the definition of minimal separation impedance (cf. eq 20 further on) that the minimal time needed to perform a given separation is determined by the minimal separation impedance \(E_{min}\) according to

\[
t_R = (N^2 \eta / \Delta p) E_{min} (1 + k')
\tag{12}
\]

Putting \(t_R\) as a fixed constant in eq 9, it follows directly that \(N\) is maximal if \(h = h_{min}\). This implies that the problem of maximizing \(N\) under the constraint of a given \(t_R\) leads to the same optimization conditions as the problem of minimizing \(t_R\) under the constraint of a given \(N\). Equation 12 then shows that the maximal number of plates (\(N_{max}\)) achievable with a fully optimized system will increase \(\sim E_{min}^{1/2}\), pointing at the potential advantage of supports with a low \(E_{min}\). At the same time, eq 12 also shows that \(N_{max} \sim \Delta p^{1/2}\), exemplifying the importance of the recently started work on ultrahigh-pressure HPLC.\(^{29}\)

2. Fixed \(d_{ref}\). In some cases, the \(d_{ref, opt}\) values determined by eq 10 can become impractically small (see 1. Free \(d_{ref}\) (i.e., \(d_{ref} = d_{ref, opt}\))). It is therefore more practically relevant to consider a fixed solid size, imposed by the fabrication or mechanical stability limits. In this case, \(d_{ref}\) can no longer be eliminated from eq 2, and also the value of \(\pi\) in the pressure-drop constraint given by eq 6 is no longer variable. Noting that eq 6 only yields one possible solution for \(v\) for each value of \(\pi\), it can be concluded that for each given combination of \(\Delta p\), \(n\), \(\eta\), and \(D_m\) only one value for \(v\) (and hence also for \(h\)) is possible. Calculating these values for a wide range of possible \(N\) and \(d_{ref}\) values using the numerical routine discussed

\(^{(26)}\) Desmet, G.; Baron, G. V. J. Chromatogr., A 2000, 867, 23–43.


below eq 6, and inserting them into the right member of eq 2, the typical Poppe plots are obtained (see further on in Figure 4). Interpreting the individual \( d_{\text{ref}} \) curves in terms of the \( \pi \) number, it should be noted that this number decreases from \( \pi \approx \pi_{\text{opt}} \) for small \( N \) to \( \pi = B \) at the vertical asymptote in the large \( N \) range. Between these two extremes, the \( d_{\text{ref}} \) constant curve touches the \( d_{\text{ref,opt}} \) limit line described by eq 12 at \( \pi = \pi_{\text{opt}} \).

Taking \( t_R \) constant in eq 2, it can again easily be understood that the conditions yielding the maximal number of plates \( N \) under the constraint of a given \( t_R \) are identical to those for the \( t_R \) minimization with a given \( N \) (in both cases \( h/v \) needs to be minimized).

3. Limited \( d_{\text{ref}} \) \((d_{\text{ref}} \geq d_{\text{ref,min}})\). The fixed \( d_{\text{ref}} \) optimization disfavors the achievable analysis time in the large \( N \) range. When approaching the vertical asymptote of the \( d_{\text{ref}} = \text{constant} \) curves, this \( d_{\text{ref}} \) value in fact becomes too small; i.e., it yields a \( \pi \) value below \( \pi_{\text{opt}} \). Assuming that it is always possible to prepare columns with the same porosity but with a larger pillar or skeleton size, \( \pi \) can again be raised, such that the system can stay away from its vertical asymptote. We therefore also conducted an optimization analysis wherein \( d_{\text{ref}} \) is allowed to be larger than the preset \( d_{\text{ref}} \) value, whenever this can yield a reduction of the analysis time.

The preset \( d_{\text{ref}} \) value is hence considered as a design minimum (referred to as \( d_{\text{ref,min}} \)): larger values are always possible, whereas smaller values are assumed to be too difficult to manufacture or too mechanically unstable. For this purpose, the optimization routine used in 2. Fixed \( d_{\text{ref}} \) has been used in a modified form, wherein \( d_{\text{ref}} \) is selected as the maximum of \( d_{\text{ref,min}} \) and \( d_{\text{ref,opt}} \).

CONSIDERED GEOMETRIES AND NUMERICAL METHODS

Figure 1 shows the unit cells for each of the different porosity systems, going from \( \epsilon = 0.3 \) to \( \epsilon = 0.9 \). Because the borders of the unit cell act as a symmetry plane (slip boundary condition for the calculation of the velocity field and zero normal concentration gradient for the calculation of the species diffusion), the flow domain behaves as if it were embedded in an infinitely replicated structure. In all the presented simulations, the total flow domain was 5 unit cells long. The drawings in Figure 1 are for a constant domain size \( d_{\text{dom}} = d_{\text{por}} + d_s \), but the simulations have also been carried out for the constant pillar size case. From the equilateral triangular arrangement of the pillars, the domain size and the length \( l \) of a unit cell can easily be shown to be given by

\[
d_{\text{dom}} = \frac{d_s}{2\sqrt{3}} \sqrt{\frac{2\pi}{1 - \epsilon}} \quad \text{and} \quad l = \sqrt{3}d_{\text{dom}} \quad (13)
\]

All relevant geometrical data are summarized in Table 1. A commercial computational fluid dynamics (CFD) software package (Fluent 6.1.22) was used for the velocity field and species
dispersion calculations. The reader is referred to refs 12 and 30 for a complete description of the employed CFD methods and the methods used to determine the plate height and permeability values. For the internal porosity ($\epsilon_{\text{int}}$) of the porous cylinders, a value of $\epsilon_{\text{int}} = 0.5$ has been adopted in all calculations. From the known external ($\epsilon$) and internal ($\epsilon_{\text{int}}$) porosities, the zone retention factor $k''$ of the unretained species (i.e., species for which $k' = 0$) can easily be calculated, using

$$k'' = \frac{1 - \epsilon}{\epsilon_{\text{int}}}$$  \hspace{1cm} (14)

All simulations were carried out with a stationary zone diffusion coefficient of $D_s = 5 \times 10^{-10}$ m$^2$/s, i.e., two times smaller than the imposed diffusivity in the through-pore region ($D_w = 1 \times 10^{-9}$ m$^2$/s). Water, with a density of 998.2 kg/m$^3$ and a viscosity of $\eta = 1 \times 10^{-3}$ kg/(m·s), was chosen as the working fluid. The phase retention factor was controlled by adapting the ratio $K$ of the forward and backward rate constants of the adsorption reaction used to mimic the retention process. From this equilibrium constant, the phase and zone retention factors ($k'$ and $k''$) can be calculated as follows:

$$k' = (1 + K)k''_0$$  \hspace{1cm} and  \hspace{1cm} $$k'' = \frac{k'' - k''_0}{1 + K}$$  \hspace{1cm} (15)

### RESULTS AND DISCUSSION

**Separation Performance Characteristics.** In Figure 2, the obtained plate height values are represented as $h = (H/d_s)$ versus $\nu = (u_0 d_{\text{ref}}/D_w)$. As is customary in the field of chromatography, $\nu$ is based on the unretained peak velocity $u_0$, which is related to the mean interstitial velocity $u$ by $u = u_0(1 + k'_0)$. Since there are two straightforward characteristic dimensions (solid size $d_s$ and domain size $d_{\text{dom}}$) to compare the different porosity systems, we found it instructive to consider both cases. Figure 2a immediately shows that the plate heights in the two domain dominated regions and in the region near $h_{\text{min}}$ strongly increase with increasing porosity in the constant solid size case. This behavior of course simply reflects the fact that, under the constant solid size assumption, increasing porosity has to be achieved by increasing the distance between the solid structures. This obviously increases the mass-transfer resistance. Figure 2a clearly shows that, if two monoliths are compared for the same skeleton size (and the same $k'$), it is straightforward to expect that the one with the largest porosity will yield significantly larger plate heights. Considering the constant domain size case (Figure 2b) on the other hand, it is striking to note that all $h$ curves lie in a relatively narrow band (except the $\epsilon = 0.9$ case). The currently presented data hence provide a powerful support for the usefulness of the domain size to compare systems with a different porosity as proposed by Minakuchi et al.\(^{32,33}\) In ref 34, a similar observation was made for 3-D structures with comparable porosities.

To translate the obtained plate height data into a suitable correlation and to gain insight in the porosity dependency of the different plate height contributions, the data shown in Figure 2 have been fitted with a $n = \frac{2}{3}$-exponent Knox equation (eq 5).\(^{32,34}\) Knox equations with $n = 0$, $n = \frac{1}{3}$, $n = \frac{1}{2}$ and $n = 1$ all yielded worse fittings, especially for the higher porosities. The resulting fitted $A$, $B$, and $C$ values are given in Table 2. As can be noted, the $d_{\text{dom}}$-based $A$ and $C$ values display a weaker dependency on $\epsilon$ than the $d_s$ reduced values, in obvious agreement with the fact

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**Table 1. Geometrical Parameters and Zone Retention Factors for the 2-D Arrays Shown in Figure 1**

<table>
<thead>
<tr>
<th>$\epsilon$ (/)</th>
<th>$d_{\text{dom}}$ (µm)</th>
<th>$l$ (µm)</th>
<th>$k''_0$ (/)</th>
<th>$k''$ (/)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.3</td>
<td>1.138</td>
<td>1.971</td>
<td>1.167</td>
<td>3.875</td>
</tr>
<tr>
<td>0.4</td>
<td>1.229</td>
<td>2.129</td>
<td>0.750</td>
<td>2.938</td>
</tr>
<tr>
<td>0.5</td>
<td>1.347</td>
<td>2.333</td>
<td>0.500</td>
<td>2.375</td>
</tr>
<tr>
<td>0.6</td>
<td>1.506</td>
<td>2.688</td>
<td>0.333</td>
<td>2.000</td>
</tr>
<tr>
<td>0.7</td>
<td>1.739</td>
<td>3.011</td>
<td>0.214</td>
<td>1.732</td>
</tr>
<tr>
<td>0.8</td>
<td>2.129</td>
<td>3.688</td>
<td>0.125</td>
<td>1.531</td>
</tr>
<tr>
<td>0.9</td>
<td>3.011</td>
<td>5.216</td>
<td>0.056</td>
<td>1.375</td>
</tr>
</tbody>
</table>

*The cited $d_{\text{dom}}$ and $l$ values are for the case of a constant solid zone diameter ($d = 1$ µm). The $k''_0$ values were calculated using eq 14. The $k''$ values were subsequently determined from eq 15 so that the phase retention factor $k'$ was the same ($k' = 1.25$) for all porosities.*

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that the $h$ curves in Figure 2 lie much closer to each other in the $d_{\text{dom}}$-reduced case than in the $d$-reduced case. The fitted $B$ values for the $d_{\text{dom}}$ reduced and the $d$ reduced case are nearly perfectly identical, in agreement with the fact that the $B$ term contribution is known to be independent of any characteristic dimension.\textsuperscript{21,31} For the cases with $0.3 \leq \varepsilon \leq 0.5$, the fitted $B$ values also lie very close (difference is $\sim 1\%$ and less) to the theoretical $B$ value, given by\textsuperscript{31}

$$B_{\text{theo}} = \frac{2}{(1 + k''_0)} \left( 1 + k'' D_{\text{r}} / D_{\text{m}} \right)$$  \hfill (16)

This agreement obviously serves as an additional validation of the employed numerical methods. For larger $\varepsilon$, the deviation between the fitted and the theoretical $B$ values is however quite significant, a phenomenon observed earlier\textsuperscript{12,30,35} for other ordered packing systems. It should be noted that this discrepancy is not due to a lack of accuracy of the employed CFD method, but to the fact that eq 5 is only an empirical approximation, originally devised for the $\varepsilon = 0.4$ packed bed, and apparently not perfectly fitting in the large $\varepsilon$ range. For the parallel plate array, for which the $h$ expression is exactly known, the $B$ value obtained by fitting the analytical $h$ expression to the $h$ curve computed with the same methods as used in the present study agreed with the theoretically expected $B$ value to within less than 0.2%.\textsuperscript{35}

The $A$ values in Table 2 clearly increase with $\varepsilon$ in both the $d$-based (strong increase) and the $d_{\text{dom}}$-based case (weaker increase). Noting that the mobile-phase mass-transfer distance grows with increasing $\varepsilon$, growing stronger in the $d$-based case than in the $d_{\text{dom}}$-based case, this clearly shows that the $A$ term is partly influenced by the mobile-phase mass transfer, in agreement with Giddings' coupling theory.\textsuperscript{36} The obtained $A$ values obviously are much smaller than those typically obtained in real packed-bed and monolithic columns. As already remarked previously,\textsuperscript{12,23,30} these low values simply reflect the high degree of packing homogeneity of the presently considered 2-D arrays. We think that no special conclusions should be drawn from the fact that the $C$ values increase with $\varepsilon$ in the $d$-based case and decrease with $\varepsilon$ in the $d_{\text{dom}}$-based case. We think it simply reflects that neither $d$ nor $d_{\text{dom}}$ is the perfect reduction basis, that the Knox plate height correlation (cf. eq 5) is only an approximation, or both.

In Figure 3, the main separation performance characteristics of the different porosity systems are shown as a function of $\varepsilon$. As we did not want to limit the present optimization study to the artificial ordered media in Figure 1, we found it instructive to compare them with the performance parameters that can be expected in a system with a strong pore heterogeneity effect, as is the case in real chromatographic media.\textsuperscript{22} For this purpose, we established a series of plate height data using the $B$ and $C$ values of the ordered case, but with a fixed amount (0.25 to be precise) added to the $d_{\text{dom}}$-reduced $A$ value. Adopting this approach, it is assumed that the multipath effect in real chromatographic packings is more or less independent of the porosity. It should be noted that the thus established disordered packing data have only been added to qualitatively demonstrate how pore heterogeneity effects influence the optimization procedures and not to exactly predict the band broadening in real packings. For the flow resistance, a survey of the literature data on the flow resistance of silica monoliths essentially revealed a large scatter, with the single general conclusion that the packing heterogeneity has the tendency to slightly reduce the flow resistance as compared to that of a perfectly ordered packing.\textsuperscript{27} To be on the safe side, we therefore put $\phi_{\text{disorder}} = \phi_{\text{order}}$.

Considering the ordered packing data shown in Figure 3a, the $h_{\text{min}}$ values clearly increase monotonically with $\varepsilon$ in the $d$-reduced case, whereas the $h_{\text{min}}$ values are nearly completely independent of $\varepsilon$ in the $d_{\text{dom}}$ reduced case. The artificially obtained disordered packing data obviously also yield $h_{\text{min}}$ values that are nearly independent of $\varepsilon$ in the $d_{\text{dom}}$ reduced case. The obtained values ($1.5 < h_{\text{min}} < 1.6$) agree well with the experimental data found in the literature, both in the small and in the large $\varepsilon$ range, hence validating the use of the 0.25 increment. For $\varepsilon = 0.4$, it is well known for packed beds that $H_{\text{min}} = 2d_{p}$.\textsuperscript{31} Assuming that the pore size in a packed bed is about one-third of the particle diameter, the corresponding domain size is equal to $d_{\text{dom}} = \varepsilon / 3d_{p}$, yielding $h_{\text{min}} = 1.5$. For $\varepsilon = 0.65$, the MS-PTFE (B) column in ref 7 produced an $H_{\text{min}}$ of $\sim 7 \mu$m ($d_{\text{dom}} = 3.85 \mu$m), corresponding to $h_{\text{min}} = 1.8$. For $\varepsilon = 0.86$, the MS (50)-A column in ref 8 yields an $H_{\text{min}}$ of $\sim 12 \mu$m for a $d_{\text{dom}} = 10 \mu$m, yielding $h_{\text{min}} = 1.2$. Obviously, these data are highly scattered and relate to different degrees of packing uniformity, but they confirm the general picture that the $d_{\text{dom}}$-based $h_{\text{min}}$ values can be expected to vary only slightly over the entire porosity range.

From Figure 3b, it can only be concluded that $v_{\text{opt}}$ decreases with increasing $\varepsilon$ in the large $\varepsilon$ range. Similar to the $h_{\text{min}}$ data, the $d_{\text{dom}}$ reduced $v_{\text{opt}}$ data are again less sensitive to changes in $\varepsilon$ than the $d$ reduced data. Another observation from Figure 3b is that the $v_{\text{opt}}$ values for the disordered packing case are smaller than for the ordered packing case, in agreement with one’s physical expectations. From the different trends for $h_{\text{min}}$ and $v_{\text{opt}}$ in Figure 3a,b, it can be inferred that the product of $h_{\text{min}}$ and $v_{\text{opt}}$ depends only very weakly on $\varepsilon$. This is clearly confirmed in Figure 3c.

\footnotesize

\begin{table}
\centering
\begin{tabular}{cccccccc}
\hline
& $d_{\text{reduced}}$ & & & $d_{\text{dom}}$-reduced & & \\
\hline
$\varepsilon$ ($/\!\!/$) & $A_{\varepsilon}$ ($/\!\!/$) & $B_{\varepsilon}$ ($/\!\!/$) & $C_{\varepsilon}$ ($/\!\!/$) & $A_{\text{dom}}$ ($/\!\!/$) & $B_{\text{dom}}$ ($/\!\!/$) & $C_{\text{dom}}$ ($/\!\!/$) & $B_{\text{theo}}$ ($/\!\!/$) \\
\hline
0.3 & 0.024 & 2.741 & 0.051 & 0.019 & 2.741 & 0.039 & 2.712 \\
0.4 & 0.035 & 2.842 & 0.053 & 0.025 & 2.842 & 0.035 & 2.821 \\
0.5 & 0.057 & 2.918 & 0.056 & 0.035 & 2.918 & 0.031 & 2.917 \\
0.6 & 0.106 & 2.816 & 0.058 & 0.054 & 2.816 & 0.026 & 3.000 \\
0.7 & 0.173 & 2.796 & 0.070 & 0.069 & 2.796 & 0.023 & 3.074 \\
0.8 & 0.333 & 2.495 & 0.094 & 0.094 & 2.495 & 0.021 & 3.139 \\
0.9 & 0.901 & 2.102 & 0.161 & 0.141 & 2.103 & 0.019 & 3.197 \\
\hline
\end{tabular}
\caption{Knox Parameters for the Considered Structures Obtained by Fitting Eq 5 (with $n = 3/2$) to the Computed $h$ Curves Shown in Figure 2a ($d$, Reduced Case) and Figure 2b ($d_{\text{dom}}$ Reduced Case)$^{a}$}
\end{table}

\footnotesize

\begin{itemize}
\item[(a)] $B_{\text{theo}}$ has been calculated on the basis of eq 16, using the $k''$ and $k''_0$ values given in Table 1.
\end{itemize}

\end{document}
the ordered and disordered case data lie very close to each other, it can also be concluded that this product also only depends very weakly on the degree of pore heterogeneity. The $h_{\min} \nu_{\text{opt}}$ data in fact also lie very close to those of the parallel plate case. It hence seems that this product is some kind of a universal constant. The fact that this constant can be calculated without having to make any assumption on the characteristic reduction basis adds to the universality of this parameter:

$$h_{\min} \nu_{\text{opt}} = \frac{H_{\min} \nu_{\text{opt}} D_{\text{ref}}}{d_{\text{ref}}} = \frac{H_{\min} \nu_{\text{opt}}}{D_{\text{m}}}$$  \hspace{1cm} (17)

This also explains why the $d_{\text{dom}}$ and the $d_s$ reduced data perfectly coincide. In fact, the very weak dependency of the $h_{\min} \nu_{\text{opt}}$ product on the porosity and the degree of packing heterogeneity can be inferred from the open-tubular LC case, for which it is well known that\(^{(38)}\)

$$h = \frac{B}{\nu} + (C_m + C_s) \nu$$  \hspace{1cm} (18)

From eq 18, it can be relatively easy shown that

$$h_{\min} \nu_{\text{opt}} = 2B_{\text{theo}}$$  \hspace{1cm} (19)

a result that is independent of the pore heterogeneity. The only difference between the particulate and monolithic supports considered in the present study and the open-tubular systems is the presence of an $A$ term in the van Deemter equation. This $A$

term contribution is, however, still relatively small near \( \nu_{\text{opt}} \), explaining why the \( h_{\min \nu_{\text{opt}}} \) product for the cylinder array only slightly deviates from this open-tubular value. It is perhaps also interesting to note that the small \( \epsilon \) supports yield \( h_{\min \nu_{\text{opt}}} \) values that are slightly larger than \( 2B_{\text{tubo}} \), whereas the large \( \epsilon \) supports yield values that are slightly smaller.

Another essential parameter determining the performance of a chromatographic system is the flow resistance. Putting \( d_{\text{rel}} = d_{\text{diam}} \) or \( d_{\text{rel}} = d_i \) in eq 4b obviously yields two different \( \phi \) values. As can be noted from Figure 3d, the \( d_{\text{diam}} \)-based flow resistance depends slightly less on the porosity than the \( d_i \)-based flow resistance. The decreasing trend is, however, present in both cases and is in full agreement with one’s physical expectations. The decreasing trend is also similar to that obtained with a computer-generated tetrahedral skeleton structure mimicking the 3-D spongelike structure of monolithic silica columns.37

Combining the \( h_{\min} \) and the \( \phi \) data, it is straightforward to calculate the minimal separation impedance \( E_{\min} \), using

\[
E_{\min} = h_{\min}^{-2} \phi
\]

(20)

\( E_{\min} \) measures the retention time per plate times the pressure drop per plate and divided by the eluent viscosity\(^{17,19} \) and is, due to its definition, independent of the selected reduction basis. From the latter, it is obvious to find that the \( d_i \) and \( d_{\text{diam}} \) reduced cases perfectly coincide. It is also obvious to find that \( E_{\min} \) is larger for the disordered case: it simply reflects that the \( h_{\min} \) values shown in Figure 3a are larger for the disordered than for the ordered packing case. It is also interesting to note that the \( (\epsilon, E_{\min}) \) relationship displays no minimum but decreases monotonically with \( \epsilon \) in both the ordered and the disordered packing cases, implying that \( h_{\min}^{-2} \) decreases less strongly with \( \epsilon \) than the decrease of \( \phi \) with \( \epsilon \). Why this is actually so is difficult to say, but it certainly points at the fact that large porosity systems benefit more from their reduced flow resistance than that they are handicapped by their larger plate heights. The continuous decrease of \( E_{\min} \) with \( \epsilon \) is also consistent with the experimental findings: the \( \epsilon = 0.4 \) packed bed yields an \( E_{\min} \) of \( \approx 2000 \)\(^{17} \) the \( \epsilon = 0.65 \) monoliths yield an \( E_{\min} \) of \( \approx 400 \)\(^{11} \) whereas a \( \epsilon = 0.86 \) monolith can produce \( E_{\min} \) values as small as 100.\(^8 \) It should also be noted that these values match nicely with the disordered case data presented in Figure 3d (dashed curve).

**Optimization Results.** As has been demonstrated in Considered Optimization Problems, the problem of minimizing \( t_k \) under the constraint of a given \( N \) and the problem of maximizing \( N \) for a given \( t_k \) are equivalent and lead to the same optimization rules. We therefore only represented the results of the minimal \( t_k \) optimization in the figures below. The information of \( N_{\text{max}} \) versus \( t_k \) can be assessed by switching the axis of \( (N,t_k) \) graphs or by following the \( t_k = \text{constant} \) lines in the \( (N,t_k/N) \) graphs. As it is thought that the particle or skeleton diameter is the characteristic dimension subjected to the most tight manufacturing or synthesis constraints, all optimization exercises discussed below have been carried out with \( d_{\text{rel}} = d_i \).

1. **Free \( d_i \) (i.e., \( d_i = d_{i,\text{opt}} \)).** With the analysis time given by eq 12, and from the fact that \( E_{\min} \) continuously decreases with increasing \( \epsilon \) (cf. Figure 3e), it can immediately be concluded that the most open porous structure will yield the shortest analysis time, independent of the required plate number. In fact, the potential reduction of the analysis time corresponds exactly to the ratio of the different \( E_{\min} \) values shown in Figure 3e. As can be seen, this gain could be very significant (roughly a factor of 10–20 if going from \( \epsilon = 0.4 \) to \( \epsilon = 0.9 \)).

From the equivalence between the \( t_{\min} \) problem and the \( N_{\text{max}} \) problem demonstrated in 1. Free \( d_{\text{rel}} \), it follows that eq 10 still determines the optimal packing dimensions. From the fact that \( N_{\text{max}} \approx E_{\min}^{-1/2} \) and that \( E_{\min} \) decreases with roughly a factor 10–20 when going from \( \epsilon = 0.4 \) to \( \epsilon = 0.9 \) in both the ordered and disordered packing cases (cf. Figure 3e), it follows that an increase in plate number of maximally a factor of 4–5 can ever be expected from the use of highly open-porous packings. The shift between the ordered and the disordered case data shows that an additional factor of 4 in \( E_{\min} \) value (i.e., a factor of 2 in \( N_{\text{max}} \)) can be expected from an increased order of the packing. Combining then the advantages of an increased porosity and of an increased packing homogeneity, it follows that maximally a factor 8–10 in plate number, i.e., a factor of \( \approx 2 \) in peak capacity \( n_p \) (\( n_p \approx N^{1/2} \))\(^{39} \) can be expected by going from a disordered system with \( \epsilon = 0.4 \) (packed bed) to a perfectly ordered system with \( \epsilon = 0.9 \).

Of course, other degrees of heterogeneity can also be considered: the larger the value of the fixed increment in the \( A \) term, the larger the heterogeneity and the larger the shift in \( E_{\min} \) will become.

Since the current optimization exercise is conducted without any restriction on the value of \( d_i \) or \( L \), it should be checked whether the corresponding \( d_{i,\text{opt}} \) values yielding the above cited gains are practically feasible. With the product of \( h_{\min} \) and \( \nu_{\text{opt}} \) being nearly perfectly constant (cf. Figure 3c), it follows from eq 10 that \( d_{i,\text{opt}} \approx \phi^{1/2} \). This shows that, since \( \phi \) decreases more than 100-fold when going from \( \epsilon = 0.4 \) to \( \epsilon = 0.9 \) (cf. the \( d_i \) case of Figure 3d), the advantage of large porosity columns should best be pursued by reducing the solid size 10-fold. For example, by assuming that \( D_k = 10^{-6} \) m\(^2\)/s and \( \eta = 10^{-3} \) kg/(m\( \cdot \)s), it can easily be calculated from eq 10 that the optimal particle or skeleton thickness of a packing with \( \epsilon = 0.4 \) is \( \approx 2 \) \( \mu \)m \( (\phi = 480) \) if \( N = 30 \) 000 plates are to be achieved, whereas the optimal particle or skeleton thickness of a packing with \( \epsilon = 0.9 \) is only \( \approx 0.15 \) \( \mu \)m \( (\phi = 3.05) \). At present, this value appears to be impractically small, such that it remains highly uncertain whether it will ever become possible to exploit the full potential of high porosity systems.

2. **Fixed \( d_i \).** Figure 4 shows a plot of the variation of \( t_k/N \) with \( N \) for two different porosities and for a number of different \( d_i \) = constant cases. Considering the \( d_i \) curves for the same porosity, the shortest analysis times are obtained in packings with small \( d_i \) in the small \( N \) range, whereas for larger plate numbers, larger \( d_i \) values are to be preferred. This was already well known for packed-bed columns,\(^{28} \) and it is no surprise to find that it holds for other porosities. The \( d_i = d_{i,\text{opt}} \) limit lines for the two different \( \epsilon \) cases run of course parallel (cf. eq 12). Comparing the \( \epsilon = 0.3 \) case with the \( \epsilon = 0.9 \) case (other cases are not represented for reasons of clarity), an important drawback of the large porosity supports becomes apparent: in the small \( N \) range, and for the same \( d_i \) value, the large \( \epsilon \) supports lead to larger analysis times (cf. the \( d_i = 1 \) \( \mu \)m curves for \( \epsilon = 0.3 \) and \( \epsilon = 0.9 \)). The only
possible way to achieve smaller analysis times with large porosity systems is to apply the available excess pressure (which stems from their smaller flow resistance) to use smaller solid sizes, if this would be practically feasible. It can, for example, be noted in the low $N$ range of Figure 4 that the $\varepsilon = 0.9$ case certainly could yield much lower analysis times than those presented. However, to achieve these low values, $d_s$ values way below 0.5 $\mu$m would be needed. As can be noted, the main advantage of a large porosity system under the condition of a given solid size is that it shifts the position of the vertical asymptote to much larger plate heights; i.e., it opens a range of large $N$ values inaccessible with small $\varepsilon$ systems.

The representation in Figure 4, however, does not yield a clear picture of which porosity yields the smallest separation time for a given required plate number. This is answered in Figure 5, where for a given solid size ($1 \mu$m) the evolution of $t_R/N$ with $N$ is given for each of the considered $\varepsilon$ values (for reasons of clarity, only one $d_s$ value is given). To assess the positions of the curves for other $d_s$ values, it should be remarked that the curves for the larger $d_s$ values are shifted to the right and the top of the graph, whereas the curves for the smaller $d_s$ values are shifted to the left and the bottom (cf. Figure 4). Figure 5 clearly shows that, for the case of a fixed pillar diameter or skeleton size, the optimal porosity gradually shifts from a small value (low permeability) for small $N$ to a large value (high permeability) for large $N$. A similar conclusion was reached by Tanaka,\textsuperscript{40} who stated that high porosity silica monoliths are only beneficial for high $N$ separations. The use of large porosity supports under the assumption of a constant $d_s$ is, hence, similar to the use of larger skeleton sizes or particles in a constant $\varepsilon$ system such as the packed bed or the $\varepsilon = 0.6$ monoliths. Similar conclusions can be drawn for the
disordered packing data (see red curves). The main difference with the ordered support data is that the individual curves are shifted upward, but this obviously is in agreement with the physical expectations. The vertical asymptote is, however, indistinguishable from the ordered support data, and the individual curves are clearly delimited by an enveloping limit. Finding an analytical expression for this limiting curve, however, appears to be much more difficult than for the limiting cases in Figure 4 and described by eq 12.

Considering the dashed $t_R = N$ = constant lines in Figure 5, it can be noted that the increase in $N_{\text{max}}$, which can be obtained by switching from an $\epsilon = 0.4$ system to a larger porosity system for $d_i = 1$ $\mu$m and for a given $t_R$ (1000 s), is a factor of $\sim 30$ for the ordered system (going from $N_{\text{max}} = 15$ 000 for $\epsilon = 0.4$ to $N_{\text{max}} = 500$ 000 for $\epsilon = 0.9$) and a factor $\sim 15$ for the disordered packing ($N_{\text{max}} = 250$ 000 for $\epsilon = 0.8$).

3. Limited $d_i$ ($d_i \geq d_{i,\text{min}}$). Figure 6 gives the results of the optimization study based on the $d_i \geq d_{i,\text{min}}$ assumption, where a lower limit is imposed on the pillar size ($d_{i,\text{min}}$) but where larger pillar sizes are permitted if they yield lower analysis times. It is found that in this case the vertical asymptotes marking the $d_i =$ constant curves in Figure 5 are replaced by $t_R \sim N^2$ lines (Figure 6a). To gain more insight in the nature of the present optimization problem, it is instructive to look at a plot of the corresponding $d_i$ values (Figure 6b). The optimization routine obviously returns $d_i = d_{i,\text{min}}$ in the small $N$ range. In this range, $\nu > \nu_{\text{opt}}$, and the $d_{i,\text{min}}$ value is larger than the optimal solid size determined by eq 10. As soon as $N$ has increased to the point where $\nu = \nu_{\text{opt}}$, the situation changes and the $d_{i,\text{min}}$ value becomes suboptimal. It can easily be inferred that, since in this case $d_i$ becomes free again, the optimization problem reduces to that of the section 1. Free $d_{i,\text{opt}}$ and the optimization routine returns the $d_{i,\text{opt}}$ values determined by eq 10. As a consequence, the $t_R/N$ curves shown in Figure 6a can be regarded as being composed of a first part matching exactly to the $t_R/N$ curves shown in Figure 5, overtaken by a second part wherein the limiting $t_R/N$ lines determined by eq 12 are followed.

The dashed $t_R = 1000$ s line in Figure 6a, shows that an increased bed porosity allows an increase in $N_{\text{max}}$ with a factor of $\sim 3.2$ for the ordered support data (going from $N_{\text{max}} = 160$ 000 for $\epsilon = 0.4$ to $N_{\text{max}} = 500$ 000 for $\epsilon = 0.9$) and a factor of $\sim 3.5$ for the disordered support data (going from $N_{\text{max}} = 70$ 000 for $\epsilon = 0.4$ to $N_{\text{max}} = 250$ 000 for $\epsilon = 0.8$). These gains translate in a gain in peak capacity of a rather disappointing value of $80\%$. Accumulating the advantage of order and large porosity, $N_{\text{max}}$ can be increased from $N_{\text{max}} = 70$ 000 for $\epsilon = 0.4$ (disordered packing) to $N_{\text{max}} = 500$ 000 for $\epsilon = 0.9$ (ordered packing) for $t_R = 1000$ s. This obviously constitutes a more significant gain in peak capacity, roughly a factor of 2.6.

Figure 6. (a) Variation of $t_R/N$ with $N$ for $d_i \geq d_{i,\text{min}}$ (with $d_{i,\text{min}} = 1$ $\mu$m) for the ordered (black lines) and the disordered packing case (red lines) and for all different considered porosities ($\epsilon = 0.3$ to $\epsilon = 0.9$). The dashed lines represent the constant $t_R$ conditions. (b) Corresponding $d_i$ values. (c) Corresponding column lengths. (d) Influence of $\Delta \rho$ on the $t_R/N$ curves for the $d_i =$ constant (dashed lines) and for the $d_i \geq d_{i,\text{min}}$ problem (full lines) for $\epsilon = 0.6$ and $d_{i,\text{min}} = 1$ $\mu$m. Other parameter values as in Figure 4. Origin of disordered packing data: see caption of Figure 3.
Figure 7. Variation of $\epsilon_{\text{opt}}$ with $N$ for different $d_{\text{min}}$ values and for the ordered (full lines) and the disordered packing case (dashed lines). Same parameter values as in Figure 4. Origin of disordered packing data: see caption of Figure 3. Symbols: $d_i \geq 1 \mu$m (●), $d_i \geq 2 \mu$m (▲), $d_i \geq 3 \mu$m (●), $d_i \geq 4 \mu$m (□), and $d_i \geq 5 \mu$m (△).

Figure 6c shows that the above-cited gain factors can only be obtained if relatively long columns (up to 0.5 m and beyond) are used. As could be expected, these lengths increase with increasing pore heterogeneity (roughly a factor of 2). Since all the curves presented thus far are for $\Delta p = 200$ bar, Figure 6d has been added to demonstrate the influence of the available inlet pressure on the achievable performances. The $t_b$ values are obviously independent of $\Delta p$ in the small $N$ limit, both for the $d_i = 1 \mu$m problem and for the $d_i \geq d_{\text{min}}$ problem. In the large $N$ range, the vertical asymptote ($d_i = 1 \mu$m constant problem) and the $t_b \sim N^2$ asymptote ($d_i \geq d_{\text{min}}$ problem) shift horizontally (see arrows in Figure 6d) in proportion with the change in $\Delta p$, in agreement respectively with eq 8 and eq 10.

Returning to Figure 6a, it can be seen that for the perfectly ordered system the large porosity supports with $\epsilon = 0.8$ become advantageous for $N_{\text{crit}} > 100$ 000 and that $\epsilon = 0.9$ packings are to be preferred as soon as $N_{\text{crit}} > 410$ 000 plates are needed. As can be noted from the red curves, the pore heterogeneity effect reduces this critical plate number. With the disordered packing plate height data considered in the present study, the $\epsilon = 0.8$ porosity is already advantageous from $N_{\text{crit}} = 70$ 000, and the $\epsilon = 0.9$ porosity should be preferred if $N_{\text{crit}} > 300$ 000. Obviously $N_{\text{crit}}$ increases with increasing $\epsilon$. Showing a plot of the packing porosity as a function of these critical $N$ values, Figure 7 shows how the packing porosity should be selected as a function of the desired plate number. This exercise was not only performed for the $d_i \geq 1 \mu$m case shown in Figure 6, but also for other values of $d_{\text{min}}$. From Figure 7, it can be observed that roughly $\epsilon_{\text{opt}} \sim \log(N)$ and that the ordered and disordered support curves run fairly parallel. Typically, the pore heterogeneity effect increases the optimal $\epsilon$ value with $\sim 0.025$ porosity unit in the high $N$ region up to $\sim 0.06$ porosity unit in the low $N$ region. The fact that $\epsilon_{\text{opt}}$ decreases with increasing $d_{\text{min}}$ is in agreement with the fact that larger $d_i$ systems already have a higher permeability and, hence, do not have to rely on a porosity increase as much as the small $d_i$ systems. For rapid separations requiring only a small number of plates, as is usually the case in the second dimension of 2-D LC systems, the optimal bed porosity obviously does not exceed a value of $\epsilon = 0.5$.

**CONCLUSIONS**

The currently presented ordered 2-D array plate height data (variable $\epsilon$, constant $k'$, and $D_s$ and $D_m$) provide a powerful support for the usefulness of the domain size as a suitable plate height reduction basis. For the same degree of packing uniformity, the $d_{\text{min}}$-based reduced plate heights vary only weakly with $\epsilon$ and can be expected to lie around $h_{\text{min}} = 0.7–0.9$ for perfectly ordered support structures and around $h_{\text{min}} = 1.5–1.6$ for the best possible real (disordered) support structures.

To benefit maximally from the reduced flow resistance of large porosity supports, submicrometer solid sizes are needed. If this could be practically realized, the maximal increase in plate number ever to be expected by raising the bed porosity from the traditional packed bed value of $\epsilon = 0.4$ to the $\epsilon = 0.9$ value of highly open-porous support structures would be maximally a factor of 4–5. With the peak capacity being proportional to $N^{1/2}$, this only gives prospect to a doubling of the peak capacity over that of the packed-bed limit, certainly insufficient to achieve the over 1000 component separations needed in the proteomics field. Putting a lower limit of $d_i = 1 \mu$m on the solid feature sizes, the potential gain in peak capacity is even smaller, and the packing homogeneity becomes more important (maximal gain in peak capacity for the disordered support case is only 80% under the condition of $t_b = 1000$ s).

Approaches combining an increased porosity with an increased packing order could maximally yield a 3-fold increase of the peak capacity over the current packed-bed capacity. If larger gains are desired, solutions as proposed in the work on ultrahigh-pressure HPLC will have to be pursued. It should also be remarked that switching to large porosity packings, for example, in the case of reversed-phase LC, usually also implies an increase of the mobile-phase viscosity to keep the retention factor $k'$ constant. This will of course further reduce the above-cited gains.

Imposing a lower limit on the useable or producible solid feature sizes, the highly open-porous support structures lose a large part of their maximal analysis speed in the small $N$ range. As a consequence, the following design rule is obtained when $L$ is free: small $N$ separations can best be performed with a small porosity packing, whereas large $N$ separations can best be performed with a large porosity packing. A plot yielding $\epsilon_{\text{opt}}$ as a function of the required plate number and the solid size has been established for the free $L$ optimization, showing that the $\epsilon_{\text{opt}}$ value roughly varies according to $\epsilon_{\text{opt}} \sim \log(N)$ in both the ordered and disordered support cases and for all possible values of $d_{\text{min}}$.

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GLOSSARY

A, B, C constants in reduced Knox equation, see eq 5 (/)
\( A_{\text{disorder}} \) artificial A term for disordered systems, obtained by adding 0.25 to \( A_{\text{order}} \) (/)
\( A_{\text{order}} \) fitted A term for ordered systems (/)
\( C_m \) mobile zone mass-transfer resistance constant in reduced van Deemter equation (/)
\( C_s \) stationary zone mass-transfer resistance constant in reduced van Deemter equation (/)
\( D_m \) molecular diffusion coefficient in mobile zone \((\text{m}^2/\text{s})\)
\( D_s \) molecular diffusion coefficient in stationary zone \((\text{m}^2/\text{s})\)
\( d_{\text{dom}} \) domain size \((d_{\text{dom}} = d_s + d_{\text{por}})\), see Figure 1a (m)
\( d_p \) particle diameter in packed bed (m)
\( d_{\text{por}} \) flow-through pore diameter (m)
\( d_{\text{ref}} \) reference length (m)
\( d_s \) solid zone diameter, see Figure 1a (m)
\( E \) separation impedance \((E = H/K_v)\) (/)
\( H \) height equivalent of a theoretical plate (m)
\( h \) reduced theoretical plate height \((h = H/d_{\text{ref}})\) (/)
\( K \) adsorption equilibrium constant (/)
\( K_v \) column permeability based on \( u_0 \) \((\text{m}^2)\)
\( k' \) phase retention factor (/)
\( k'' \) zone retention factor (/)
\( k''_0 \) zone retention factor of the unretained species (/)
\( l \) length of a computational unit cell (m)
\( L \) column length (m)
\( N \) plate number (/)
\( N_{\text{crit}} \) plate number for which a certain porosity yields the minimal analysis time (/)
\( n_p \) peak capacity (/)
\( R_s \) resolution (/)
\( t_R \) retention time (s)

\( u \) mean interstitial velocity (m/s)
\( u_0 \) mean velocity of permeating, but nonretained solute (m/s)

Greek symbols

\( \alpha \) selectivity factor, defined as the ratio of the phase retention factors of the components to be separated (/)
\( \Delta p \) pressure drop (Pa)
\( \epsilon \) extraskeleton porosity (/)
\( \epsilon_{\text{int}} \) intraskeleton porosity (/)
\( \phi \) flow resistance (/)
\( \eta \) dynamic viscosity (kg\cdotm\(^{-1}\)\cdots\(^{-1}\))
\( v \) reduced fluid velocity \((v = u(d_{\text{ref}}/D_m))\) (/)
\( \tau \) dimensionless pressure, see eq 6 (/)
\( \tau_{\text{opt}} \) dimensionless pressure corresponding to minimal analysis time, see eq 11 (/)

Subscripts

disorder data referring to support structure with a significant degree of packing heterogeneity
dom domain size-related
max maximal
min minimal
opt optimal
order data referring to the perfectly ordered solid zone arrays shown in Figure 1
s solid size-related

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