

Kinetic performance factor - A measurable metric of separation-time-pressure tradeoff in liquid and gas chromatography

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1 Specific transport efficiency – a universal metric of a column 2 structural quality in liquid and gas chromatography

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8

9 HIGHLIGHTS

10 Specific Transport Efficiency (STE) is a metric of tradeoff between time and separation

11 The larger is a column STE the larger is its peak capacity in the same time and at the same pressure

12 STE, effective diameter and nominal diffusivity are the core set of column parameters

13 Use of the core parameters for evaluation of several metrics of column performance demonstrated

Specific transport efficiency – a universal metric of a column structural quality in liquid and gas chromatography

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ABSTRACT

A metric of structural quality of a column in liquid and gas chromatography – the column specific transport efficiency (e_s) – is proposed. Measurable by identical rules for all column types (open-tubular, packed, monolithic, pillar-array, etc., regardless of retention mechanism), e_s supersedes such quality metrics as dimensionless plate height (h), Bristow-Knox separation impedance (SI), Golay specific performance index (SPI) and others. Peak capacity, and other separation performance measures of a chromatographic system are proportional to e_s . To theoretically predict the separation-time performance of a column with known e_s , two measurable parameters – a column effective diameter (d_{eff}) and nominal diffusivity (D_n) were introduced. Quantities e_s and D_n represent the properties of classes of self-similar columns while d_{eff} represents a particular column. The use of parameters d_{eff} , e_s and D_n for evaluation of relations between efficiency and void time (t_M) in columns of several types has been demonstrated. It is always more time-efficient to use maximum available instrumental pressure (Δp_{max}) for obtaining a predetermined column efficiency even if that efficiency is

24 relatively low so that operation at Δp_{\max} requires non-optimal flow. It has been also demonstrated that
25 reducing characteristics cross-sectional dimension (d_{eff} , particle size of a packed column, internal
26 diameter of and open-tubular column, etc.) of a column operating at the same Δp_{\max} reduces the
27 column efficiency with the benefit of disproportionately faster analysis.

28 **1. Introduction**

29 The key issue for this report is to identify a core set of measurable properties of LC and GC columns
30 that is sufficient for the prediction of a column general separation performance, analysis time and the
31 tradeoff between them.

32 Two types of properties of chromatographic columns – the *transport properties* and the *selectivity* –
33 can be distinguished. The latter represents a column ability to transport different solutes in different
34 times and to effect by that a column *specific separation performance* – the separation of particular
35 peak pairs. On the other hand, the transport properties are concerned with transporting each *single*
36 solute or, in the case of transporting a solute mixture, the transport properties describe the similarities
37 rather than differences in transporting different solutes. Peak capacity (n_c), column plate number (N)
38 and plate height (H) are examples of metrics of a column transport properties representing its *general*
39 *separation performance* (briefly, *separation performance*). Among other transport properties are *void*
40 *time* (t_M) and *loadability* (*sample capacity*). The former affects the *analysis time* while the latter
41 represents the largest amount of sample that can be transported through the column without distorting
42 other transport properties. While recognizing the importance of loadability, we only mention but do not
43 evaluate its effect and only evaluate the relations between the separation performance and the analysis
44 time.

45 The interdependence of a column separation performance and analysis time has been recognized
 46 since the early days of chromatography, and it enjoys significant attention in contemporary studies [1-
 47 15]. Golay was the first to recognize the interdependence in 1957 [1] together with being also the first
 48 to recognize that the tradeoff between the two is constrained by the available column pressure: “the
 49 pressure drop, is what you might call the price paid for a certain column performance” [1], “the
 50 performance index is ... a measure of ... [efficiency] with which a given *column design* achieves a
 51 certain resolution with a given pressure differential and a given time” [3].

52 The separation-time tradeoff substantially depends on a column structure. Golay demonstrated [1, 2]
 53 that, in GC, an open-tubular column (OTC) yields the same separation performance in shorter time
 54 and/or at lower pressure than a packed column does.

55 Several metrics of column performance are known in chromatography. In addition to earlier
 56 mentioned n , N and H , they include a column dimensionless plate height (h), Golay’s *specific*
 57 *performance index* (SPI) for GC columns [2], Bristow-Knox *separation impedance* (SI) for LC
 58 columns [8], and others. With so many metrics, the question of choice arises.

59 A metrics of choice in this report should be *measurable by objective external measurement of a*
 60 *column as a whole*. The objectivity means that the measurement of a particular metric should be
 61 conceptually identical for all columns and techniques. Thus, because a peak retention time (t) and
 62 standard deviation (σ) are externally measurable (briefly, *measurable*) quantities, a column *plate*
 63 *number*:

$$64 \quad N = \left(\frac{t}{\sigma} \right)^2, \quad (\text{static}) \quad (1)$$

65 in *static* chromatography [16, 17] (isothermal isobaric GC, isocratic isothermal isobaric LC, etc.) is a
 66 measurable quantity. Also measurable is a column plate height:

$$67 \quad H = \frac{L}{N} = L \left(\frac{\sigma}{t} \right)^2 \quad (2)$$

68 where a column length (L) is measurable not only because it can be measured by a ruler, but also
69 because it can be found (Supplement) from measuring a column operational parameters (without
70 “opening a column compartment” in the instrument).

71 An example of *unmeasurable (subjective)* property in the context of this report is a packed column
72 *particle size* (d_p) which cannot be found from the measurement of parameters of a column as a whole.
73 There are additional difficulties with identifying d_p for *monolithic* [18, 19], *pillar-array* [20, 21], and
74 other columns where the subjectivity arises from the need to compare intrinsically incomparable
75 spherical and non-spherical support structures. In all such cases, d_p is typically defined on the basis of
76 subjective considerations [14]. As a result, the *dimensionless plate height* of a packed column [22, 23]:

$$77 \quad h = \frac{H}{d_p}, \quad (\text{packed column}) \quad (3)$$

78 is also a subjective quantity. Additionally, the *dimensionless plate height* in an OTC is typically
79 defined as [24, 25]:

$$80 \quad h = \frac{H}{d_c}, \quad (\text{OTC}) \quad (4)$$

81 where d_c is internal diameter of a column tubing. Replacing the normalizing *characteristic cross-*
82 *sectional dimension* d_p in Eq. (3) with d_c in Eq. (4) is also subjective.

83 We identified below a core set of three intensive transport properties of chromatographic columns
84 and a corresponding core set of three measurable parameters that are sufficient for evaluating other
85 transport properties. One of the core parameters – the dimensionless *specific transport efficiency* (e_s) –
86 supersedes the earlier mentioned parameters h , SI, SPI as the metrics of a column structural quality.

87 Because the *standard deviation* (σ) is the only known measurable peak width metric that can be
88 theoretically predicted from column properties and operational conditions [26], it is the only peak
89 width metric in this report. This approach makes the result of the study applicable to all peak shapes.
90 The terms *peak standard deviation* and *peak width* are treated below as synonyms. As another

91 convention, the term retention factor (k) is synonymous in this report with what is also known as the
92 *phase retention factors* (k') [14, 27].

93 To eliminate from this study the *extra-column* factors [28] such as insufficiently sharp sample
94 introduction and limits to ability of data analysis subsystem to *resolve* (identify and quantify) closely
95 spaced peaks, we assume that the sample introduction is sufficiently **sharp** for a negligible effect on a
96 column performance, and we do not consider the specifics of the peak measurement and identification.
97 Additional assumptions introduced below are typed in the **boldface** type.

98 **2. Theory**

99 *2.1 Transport efficiency*

100 To identify the core set of intensive properties of a chromatographic column that affect its
101 performance, we first consider a broader picture.

102 The key purpose of chromatography is the *separation*. Other parameters of chromatographic analysis
103 like the *analysis time* and a column *loadability* are subordinate to the separation performance and can
104 be viewed as its price. It is important, therefore, to use the performance metrics that most transparently
105 and intuitively relate to the separation performance.

106 Several layers of general separation performance of a chromatographic system can be recognized
107 [29]. On the top is the largest statistically expected number (m) of peaks that the system can *resolve*.
108 This can be viewed as the ultimate performance metric. Below m is the *peak capacity* (n_c) [23, 30] –
109 the largest number of resolvable peaks that can be packed in the separation space of analysis.
110 According to peak overlap statistics [23, 31], m is proportional to n_c ($m \sim n_c$). Thus, when all peaks are
111 identical, $m = n_c/(2e) \approx 0.184n_c$ [23, 29, 31]. The next layer down is the column *separation capacity*
112 (s) [29, 32] – the number of σ -*slots* (σ -wide segments) along a chromatogram. Quantities n_c and s relate

113 as $n_c = s/\Delta s_{\text{req}}$ where Δs_{req} is the smallest number of σ -slots between two peaks that the data analysis
 114 subsystem requires for resolving them [29]. One has: $m \sim n_c \sim s$. The next layer down is a column plate
 115 number (N), Eq. (1). In static and *dynamic* (temperature-programmed GC, gradient LC, etc.)
 116 chromatography, quantities m , n_c and s are proportional to \sqrt{N} (the same is true for not considered
 117 here peak resolution, R_s [33], and separation, Δs [29]). The fact that N is not proportional to the key
 118 metrics of separation performance is a source of substantial disruption in the system of metrics and of
 119 frequently exaggerated significance of the values of N : “(N is an) awkward measure, as the resolving
 120 power is only proportional to the square root of the plate number” (Poppe [11]). Similar frustrations
 121 with N as a performance metric were expressed by other workers [34, 35].”

122 There are also questions about physical meaning of quantity N . Defined by widely known and
 123 IUPAC recommended [33] expression $N = (t/\sigma)^2$, Eq. (1), quantity N can be different from the actual
 124 number, L/H_{loc} , of *local plate height* (H_{loc}) units along a column. For example, due to the carrier gas
 125 compressibility, this is always the case in GC [26, 36]. Similarly, $N \neq L/H_{\text{loc}}$ in LC with non-uniform
 126 columns [37, 38], etc. A question inevitably arises: What is a rationale for parameter N that can be
 127 different from its declared physical meaning, and that is calculated as $(t/\sigma)^2$ in order to be followed by
 128 calculation of $\sqrt{(t/\sigma)^2}$ in evaluations of all known parameters of separation performance? The answer
 129 seems to be: a historically established tradition, but not a scientific reason.

130 Instead of N , a column *transport efficiency*, $E = \sqrt{N}$ [15, 17, 29, 39] (*separation power* [32, 40]),
 131 can be used. Due to Eqs. (1) and (2), quantities E and H can be defined as:

$$132 \quad E = \frac{t}{\sigma} \tag{5}$$

$$133 \quad H = \frac{L}{E^2} \tag{6}$$

134 The following observations illustrate an important aspect of proportionality of s and, therefore, of n_c
 135 and m to E .
 136 *Characteristic thermal constant* (θ_{char}) in GC [26, 39, 41, 42], and *characteristic strength constant*
 137 (Φ_{char}) in LC [15, 17, 43] play important role in these techniques. They can be estimated as
 138 $\theta_{\text{char}} \approx 30^\circ\text{C}$, $\Phi_{\text{char}} \approx 0.1$ (or 10%) in RPLC (reverse phase LC) of small molecules and $\Phi_{\text{char}} \approx \sqrt{3/M}$
 139 of large molecules having $M > 300$ (M is molecular weight). Increasing GC column temperature by
 140 θ_{char} or increasing the solvent strength in LC by Φ_{char} reduces $\ln k$ by 1. Quantity E relates to θ_{char} and
 141 Φ_{char} in the following straightforward way. In temperature-programmed GC, the incremental separation
 142 capacity (Δs) of each θ_{char} -wide temperature span is equal to E at slow heating rate and to $0.8E$ at
 143 optimal heating rate [44]. Similarly, in gradient LC, Δs of each Φ_{char} -wide solvent strength span is
 144 equal to E [17] at slow solvent strength programming, and to $0.8E$ at optimal solvent strength
 145 increasing rate [45]. In other words, there are straightforward relationships between E and the number
 146 of σ -slots in characteristic segments of the separation space in temperature-programmed GC and
 147 gradient LC. For example, In RPLC analysis of small molecules ($\Phi_{\text{char}} \approx 10\%$) at optimal solvent
 148 strength programming rate, there are approximately $0.8E$ σ -slots in each time segment corresponding to
 149 10% solvent composition change. This implies that, if a 4σ -separation is required for resolving two
 150 peaks then the incremental peak capacity (Δn_c) of each 10% solvent composition span can be estimated
 151 as $\Delta n_c \approx 0.8E/4 = 0.2E$, and the maximum peak capacity ($n_{c,\text{max}}$) of optimal programming from 0 to
 152 100% of stronger solvent is $n_{c,\text{max}} \approx 2E$.

153 Using in column performance evaluations E instead of N , extends the chain of proportionalities,
 154 $m \sim n_c \sim s$, to:

$$155 \quad m \sim n_c \sim s \sim E \quad (7)$$

156 Generally, the lower is the level of performance property the smaller is the number of factors
 157 affecting it. Thus, metrics m and n_c in the upper level depend on the column and on ability of data
 158 analysis subsystem to resolve closely spaced peaks. Metrics s and E in the next two lower levels only
 159 depend on a column and its operational conditions, but, unlike m and n_c , do not depend on the
 160 subsystems (like the data analysis subsystem) that do not control the column operation. And among
 161 metrics s and E , only the former strongly depends on the analysis time while time has no direct effect
 162 on E . All metrics in Eq. (7) represent a column *extensive* properties as all depend on the column length,
 163 and all but E depend on analysis time. Our next goal is to identify a lower level *intensive* metric that
 164 can be added to the chain in Eq. (7)..

165 2.2 Operational conditions

166 The basic definitions in this report apply to *linear* (no column overloading) LC and GC based on
 167 packed columns (conventional, *monolithic* [18, 19], *pillar-array* [20, 21], etc.) with totally or partially
 168 porous packing, and on open-tubular columns (OTC) – WCOT (wall-coated open tubular), PLOT
 169 (porous layer open-tubular), etc. with **incompressible solvent** in LC and **ideal carrier gas** in GC.

170 2.3 Transport permeability

171 Let p_i , p_o and $\Delta p = p_i - p_o$ be a column *inlet pressure*, *outlet pressure* and *pressure drop*,
 172 respectively. In a L -long column with fluid viscosity η , the *void time* (t_M) – the average time of
 173 transporting the mobile phase molecules from column inlet to outlet – can be found as [14, 26, 46]:

$$174 \quad t_M = \frac{L^2 \eta}{K_v \Delta p_{\text{eff}}} \quad (8)$$

175 where K_v is a column *transport permeability* (*chromatographic permeability* [8, 47], *permeability*
 176 *based on mean velocity of unretained solute* [14], *u_0 -based permeability* [48]), and (Δp_{eff}) is the
 177 *effective pressure* (*virtual pressure* [26]) defined as:

$$\Delta p_{\text{eff}} = \begin{cases} \Delta p, & \text{incompressible fluid} \\ j_H \Delta p, & \text{ideal gas} \end{cases} \quad (9)$$

where:

$$j_H = \frac{3(p_i + p_o)^2}{4(p_i^2 + p_i p_o + p_o^2)} \quad (10)$$

is the *Halász-Hartmann-Heine compressibility factor* [26, 49]. As parameters L , Δp_{eff} , t_M and η are measurable quantities, Eq. (8) defines quantity K_v measurable for incompressible fluid and ideal gas as:

$$K_v = \frac{L^2 \eta}{\Delta p_{\text{eff}} t_M} \quad (11)$$

In forthcoming numerical examples, we will use theoretically predicted values of measurable parameters. Thus, according to *Poiseuille law* [26, 50], K_v in an open circular tube of internal diameter d and in a packed column can be estimate as [6, 8, 14, 20, 47, 48, 51-53]:

$$K_v = \frac{d^2}{32}, \quad (\text{open circular tube}) \quad (12)$$

$$K_v = \frac{d_p^2}{\phi}, \quad (\text{packed column}) \quad (13)$$

where ϕ is the *transport resistance factor* (flow parameter [6], flow resistance factor [51, 52], dimensionless flow resistance parameter [8], column resistance factor [47], flow resistance [14, 20]).

It can be noticed that, being defined in Eq. (13) through unmeasurable quantity d_p , quantity ϕ is also unmeasurable. It is known, however, that, for a column packed with identical non-porous spherical particles of diameter d_p , quantity ϕ can be estimated as [20, 47, 48, 53]:

$$\phi \approx 400, \quad (\text{regular spherical packing}) \quad (14)$$

This estimate is used in all forthcoming numerical evaluations.

196 2.4 Effective diameter

197 The *effective transport diameter* (briefly, *effective diameter*), d_{eff} , of a L -long column (with
 198 compressible or incompressible fluid) is the internal diameter (d) of equally long open uniform inert
 199 circular reference tube with incompressible fluid that yields the same void time (t_M) as does the column
 200 when Δp and η are the same in both cases.

201 Eqs. (8), (9) and (12) yield:

$$202 \quad t_M = \frac{32L^2\eta}{d^2\Delta p}, \quad (\text{reference tube}) \quad (15)$$

203 The *definition* of d_{eff} suggests that d_{eff} is the solution of this equation for d :

$$204 \quad d_{\text{eff}} = L \sqrt{\frac{32\eta}{t_M\Delta p}} \quad (16)$$

205 As all parameters in the right hand side of this definition are measurable quantities, d_{eff} is also a
 206 *measurable* quantity. Combining the last equation with Eqs. (8) and (9), one can also express d_{eff} as:

$$207 \quad d_{\text{eff}} = \sqrt{\frac{32K_v\Delta p_{\text{eff}}}{\Delta p}} = \sqrt{32K_v} \cdot \begin{cases} 1, & \text{LC} \\ \sqrt{j_H}, & \text{GC} \end{cases} \quad (17)$$

208 It might be also convenient to replace the ratio $32\eta/\Delta p$ in some expressions with its *time-equivalent*:

$$209 \quad t_p = \frac{32\eta}{\Delta p} \quad (18)$$

210 For example, in LC with 50/50 (V/V) water/acetonitrile solvent at 25 °C, $\eta \approx 0.81$ cP [54]. At
 211 $\Delta p = 1200$ bars (close to the highest commercially available pressure), Eq. (18) yields $t_p \approx 0.22$ ns.
 212 What should be the Δp in GC to obtain the same t_p ? For hydrogen (the fastest carrier gas [26, 39]) at
 213 150 °C (approximately the middle of GC temperature range), $\eta \approx 0.0113$ cP [26]. Eq. (18) yields:
 214 $\Delta p = 16.8$ bars. Known commercial GC instruments do not supply this pressure, but mostly because
 215 there is no practical need for that as the dominant performance limit for GC WCOT columns is not

216 pressure, but detection limit [39]. Assuming that, if necessary, 20 bars and higher pressure could be
 217 available in GC, quantity:

$$218 \quad t_p = 0.2 \text{ ns} \quad (19)$$

219 is used in all forthcoming numerical examples (GC and LC) as the lowest (the best) practically
 220 available t_p .

221 With notation t_p , Eq. (16) becomes:

$$222 \quad d_{\text{eff}} = L \sqrt{\frac{t_p}{t_M}} \quad (20)$$

223 It follows from Eq. (17) that d_{eff} depends on the column structure and cross-sectional dimensions
 224 (both represented by parameter K_v). In GC, d_{eff} also depends via parameter j_H , Eq. (10), on the column
 225 inlet and outlet pressure (p_i and p_o). While expressing K_v in the form of effective diameter (d_{eff}) seems
 226 natural, defining d_{eff} as being dependent on the column operational conditions (p_i and p_o) can be
 227 questioned. Alternatively, d_{eff} could have been defined as being independent of pressure by, e.g., using
 228 in Eq. (16) Δp_{eff} instead of Δp . However, the alternative choices would spill over to other concepts
 229 introduced below either complicating them or complicating their relations.

230 2.5 Separation impedance and universal plate height

231 Let t and

$$232 \quad k = \frac{t}{t_M} - 1 \quad (21)$$

233 be a solute retention time and retention factor, respectively, in static analysis. The *separation*
 234 *impedance* (SI),

$$235 \quad \text{SI} = \frac{\Delta p t}{E^4 \eta (1 + k)}, \quad (22)$$

was introduced by Bristow and Knox [8] as a dimensionless performance measure of packed LC columns (quantity N^2 instead of E^4 was used in the source). All parameters in this definition are measurable quantities, and nothing prevents its extension to GC and LC with both, OTC and packed columns. Due to Eqs. (6), (20) and (21), SI in Eq. (22) can be expressed as:

$$SI = \frac{\Delta p t_M}{E^4 \eta} = \frac{32 t_M}{E^4 t_p} \quad (23)$$

$$SI = 32 h_U^2 \quad (24)$$

where dimensionless quantity h_U , defined as:

$$h_U = \frac{H}{d_{\text{eff}}} \quad (25)$$

can be called as the *universal plate height* – universal because a column characteristic cross-sectional dimension, d_{eff} (the normalization factor in the definition of h_U) is measured in the same way, Eq. (16), for all columns. Eqs. (17), (23), (24) and (25) allow one to express SI and t_M as:

$$SI = \frac{H^2 \Delta p}{K_v \Delta p_{\text{eff}}} = \frac{H^2}{K_v} \cdot \begin{cases} 1, & \text{LC} \\ 1/\sqrt{j_H}, & \text{GC} \end{cases} \quad (26)$$

$$t_M = SI \frac{E^4 t_p}{32} = h_U^2 E^4 t_p \quad (27)$$

Eq. (24) indicates that SI and h_U are *equivalent* to each other – a value of one uniquely determines the other. Furthermore, comparison of Eq. (24) with the definitions, Eqs. (3), (4) and (25), of h and h_U suggests that SI is nothing but a differently normalized h^2 , and that there is no conceptual difference between metrics SI and h_U on the one hand, and conventional dimensionless plate height (h) on the other. However, although the difference between h_U and h is not conceptual, it is essential. The characteristic cross-sectional dimensions (d_p and d) in the definitions, Eqs. (3) and (4), of h are different from each other. On top of that, d_p is unmeasurable and, in some cases (monolithic columns, pillar-array columns), its values is chosen arbitrarily. As a result, h is unsuitable for comparison of

columns of different type (packed and open-tubular, packed conventional and pillar-array, etc.). On the other hand, the consistent measurement of d_{eff} as a column characteristic cross-sectional dimension offers a single and objective measurable value (d_{eff}) enabling the comparison of different column types. Thus, according to Eq. (27),

any two columns operating at the same ratio $\eta/\Delta p$ and yielding the same transport efficiency (E), require the same t_M as long as both have the same h_U .

To a certain degree, the choice of d_{eff} as characteristic cross-sectional dimension for all columns is the essence of the treatment in this report.

How do the metrics SI and h_U relate to Golay's SPI (*specific performance index*) [2] for GC columns – the earliest known metric of separation-time tradeoff and the prototype for Bristow-Knox SI [8]? As shown in Supplement,

$$\text{SPI} = \frac{\text{SI}}{\text{SI}_{\text{WCOT,thin,min}}} = \left(\frac{h_U}{h_{U,\text{WCOT,thin,min}}} \right)^2 \quad (28)$$

indicating that, like h_U and SI, the SPI is just another differently normalized and/or differently powered dimensionless plate height. However, as quantities $\text{SI}_{\text{WCOT,thin,min}}$ and $h_{U,\text{WCOT,thin,min}}$ depends on a solute retention factor in a reference thin film WCOT column, SPI is not equivalent to mutually equivalent metrics h_U and SI.

2.6 Specific transport efficiency

Both metrics, SI and h_U , represent intensive properties of a column separation performance. As they are equivalent to each other, either one could be a candidate for a set of a column core parameters. However, neither is proportional (nor inversely proportional) to mutually proportional higher level metrics in Eq. (7) as, according to Eqs. (6), (24) and (25): $h_U \sim 1/E^2$, $\text{SI} \sim 1/E^4$.

278 To avoid these shortcomings, we propose a column *specific transport efficiency* (briefly, *specific*
 279 *efficiency*) defined as:

$$280 \quad e_s = \sqrt{\frac{d_{\text{eff}}}{H}} \quad (29)$$

281 It follows from Eqs. (6), (7), (24) and (25) that e_s is proportional to E and, therefore,

$$282 \quad m \sim n_c \sim s \sim E \sim e_s \quad (30)$$

283 While satisfying this proportionality chain, e_s is *equivalent* to h_U and SI relating to them as:

$$284 \quad e_s = \frac{1}{\sqrt{h_U}} = 2 \left(\frac{2}{\text{SI}} \right)^{1/4} \quad (31)$$

285 Due to Eqs. (5), (6), (18), (20) and (29), e_s can be expressed as a functions of directly measurable
 286 parameters Δp , t , t_M , η and σ :

$$287 \quad e_s = E \sqrt{\frac{d_{\text{eff}}}{L}} = \frac{t}{\sigma} \left(\frac{t_p}{t_M} \right)^{\frac{1}{4}} = \frac{t}{\sigma} \left(\frac{32\eta}{\Delta p t_M} \right)^{\frac{1}{4}} \quad (32)$$

288 One can use the right hand side of this expression to plot a function $e_s(u)$ where $u = L/t_M$. It follows
 289 from the definition of e_s in Eq. (29) that $e_s(u)$ has a maximum ($e_{s,\text{max}}$) at u_{opt} corresponding to H_{min} .

290 Using e_s , Eq. (27) can be expressed as:

$$291 \quad t_M = \left(\frac{E}{e_s} \right)^4 t_p, \quad \text{or} \quad \frac{t_M}{t_p} = \left(\frac{E}{e_s} \right)^4 \quad (33)$$

292 implying that E and, therefore, other metrics in Eq. (30) are proportional to e_s when Δp and t_M are

293 fixed. The last equation also indicates that e_s is the transport efficiency (E) per unit of $(t_M/t_p)^{1/4}$

294 justifying naming e_s as the *specific* transport efficiency. Being a monotonically declining function of

295 H , Eq. (29), quantity e_s has the maximum ($e_{s,\text{max}}$) at optimal flow rate (F_{opt}) where H has the minimum.

296 The optimal t_M and E corresponding to F_{opt} are denoted here as $t_{M,\text{Opt}}$ and E_{Opt} where the purpose of the

capital “O” in the subscript “Opt” is to distinguish the fact that quantities $t_{M,Opt}$ and E_{Opt} correspond to two conditions: optimal flow rate (F_{opt}) and fixed pressure drop (Δp).

The properties in Eq. (30) are arranged in the order of decreasing their level from left to right. An improvement in performance on some level improves the performance on all higher levels. As $e_{s,max}$ is the metric of the lowest level in the chain, its improvement improves the performance metrics on all other levels. Thus, increasing e_s by, say, a factor of two, increases E at a fixed Δp and t_M as well as all other metrics in Eq. (30) by the same factor of two. If raising e_s is not dictated by the need to increase all other performance metrics then, according to Eq. (33), the larger e_s at fixed Δp and E can be used for reducing the analysis time in inverse proportions to e_s^4 . Thus, doubling e_s without changing Δp and E makes t_M 16 times shorter. As it depends on a column structure, and as it effects all other performance metrics of a column, quantity $e_{s,max}$ can be viewed as a measure of *structural transport quality* of a column design – representing relative sharpness of chromatographic peaks that different column designs can deliver under comparable conditions. The larger is $e_{s,max}$ the better is the quality and the better are all other performance metrics under otherwise identical conditions.

Quantity $e_{s,max}$ can be used for comparison of the separation-time performance of columns of different structures (conventional packed, monolithic, pillar-array, PLOT, etc.), different ways of raising column loadability (by, say, raising porosity of support structure, or by increasing a column tubing diameter without changing the support structure [55]), different orientation of internal pores (say, random or radial [56]), etc.

2.7 Attainable performance

Parameter e_s quantifies the tradeoff between the column transport efficiency (E) and the void time (t_M). However, it does not say what actually a given column can deliver. Can it deliver, e.g., $E = 1000$? Under what conditions? Some of these issues were addressed in the literature separately for GC [39]

and LC [45]. Here they are evaluated from a single perspective. Recognizing that other extensive properties in Eq. (30) are proportional to E and that the analysis time is proportional to t_M , we only evaluate below E and t_M .

Let u and u_{opt} be, respectively, the *velocity* of transporting mobile phase molecules along the column and its optimum corresponding to the minimum (H_{min}) in H and, therefore, to the minima in h_U and SI and to the maximum ($e_{s,\text{max}}$) in e_s . How u_{opt} can be predicted from a column measurable parameters?

Quantity u_{opt} strongly depends on a column characteristic cross-sectional dimension being, in general, inversely proportional to it [17]. As a result, the product $d_{\text{eff}}u_{\text{opt}}$ for a given solute, mobile phase and conditions is more or less independent of d_{eff} . To formalize these observations, we extend the concept of *self-similar* packed LC columns [14, 15] to arbitrary LC and GC ones. Extending the GC *method translation* concept [26, 57] to LC, we define that two columns are *translations* of each other if retention factor of any solute is the same in both columns. A column plate height can be described [15, 26, 39] as a function of the ratio u/u_{opt} . For example, it can be verified by direct substitution of parameters in Eq. (35) into Eq. (34) that van Deemter equation $H = A + B/u + Cu$ for a packed LC column can be expressed as a function of its optimal parameters u_{opt} and H_{min} :

$$H = H_{\text{min}} \left(a + \frac{1-a}{2} \left(\frac{u_{\text{opt}}}{u} + \frac{u}{u_{\text{opt}}} \right) \right) \quad (34)$$

$$H_{\text{min}} = A + 2\sqrt{BC}, \quad a = \frac{A}{H_{\text{min}}}, \quad u_{\text{opt}} = \sqrt{\frac{B}{C}} \quad (35)$$

Eq. (34) also applies to thin film WCOT GC columns [26, 39] for which $a = 0$. Two columns are said to be *self-similar* [15] if they are translations of each other, and if for any solute under identical conditions in both columns:

- the product $d_{\text{eff}}u_{\text{opt}}$ is the same

- h_U (and, therefore, e_s) is the same when the ratio u/u_{opt} is the same

Mutual translatability of two columns is the key requirement for a practical method transfer, as it preserves the relative retention of all peaks. If two mutually translatable columns are not self-similar, different transport efficiency might be required for obtaining a necessary separation of the target peak pairs. The efficiency can be adjusted by choosing a proper column length in each case [26, 57].

Returning to column parameters affecting u_{opt} , let's define two quantities:

$$D_{np} = \frac{d_{eff} u_{opt}}{2} \quad (36)$$

$$D_n = D_{np} \cdot \begin{cases} 1, & \text{LC} \\ p/p_{st}, & \text{GC} \end{cases} \quad (37)$$

where $p_{st} = 1$ atm (*standard pressure*). Both quantities are measured in units of diffusivity (length²/time). We will call D_n as the *nominal diffusivity* (of a given solute in a given column and the mobile phase). There is no difference between D_{np} and D_n in LC. In GC, D_{np} is measured at the same pressure as is u_{opt} while D_n is D_{np} rescaled to 1 atm. As D_n for a given solute and mobile phase is the same for all self-similar columns, it can be used for evaluation of u_{opt} in a column with particular d_{eff} . As u_{opt} is approximately proportional to a solute molecular diffusivity (D_m), quantities D_{np} and D_n are also approximately proportional to D_m . For example, in a thin film WCOT column, $u_{opt} \approx 5.5 D_m / d$ at $k = 2$ [26]. From Eqs. (10), (12), (13) (14), (17) and (37), one can find that D_n in GC-MS can be estimated as $D_n \approx 2.4 D_{m,st}$ where $D_{m,st}$ is D_m at 1 atm. For a solute eluting with $k = 2$ from a typical column with hydrogen at 150 °C, this yields $D_n \approx 1.3 \text{ cm}^2/\text{s}$ [26]. For LC columns with spherical packing, u_{opt} can be estimated as [48, 58] $u_{opt} \approx 10 D_m / d_p$ leading to $D_n \approx 1.4 D_m$. For small molecules in LC, D_m can be approximated as $D_m = 10^{-5} \text{ cm}^2/\text{s}$ [58, 59] leading to $D_n \approx 1.4 \times 10^{-5} \text{ cm}^2/\text{s}$. The values:

$$D_{n,GC} \approx 1.3 \text{ cm}^2/\text{s}, \quad D_{n,LC} \approx 1.4 \times 10^{-5} \text{ cm}^2/\text{s} \quad (38)$$

are used in forthcoming numerical examples.

Since D_m is a function of a solute molecular size [60, 61], it covers a relatively wide range especially in LC. The same is true for D_n , approximately proportional to D_m . As a result, D_n in a given column is a solute-dependent parameter and cannot be treated as a column parameter. When D_n of two columns is compared in this report, the same solute is always assumed.

On the other hand, the proportionality of D_n to D_m in a given class of self-similar columns suggests that their ratio D_n/D_m might represent a solute-independent property of the class. The *dimensionless mobile phase velocity*, $v = \underline{u}d_p/D_m$ introduced by Giddings [22, 62] for packed columns might serve as a prototype for the metric of that property. The reason for not directly using v as such metric is that, being a function d_p , quantity v is not a measurable parameter. This problem is avoided in dimensionless quantity:

$$v_U = \frac{d_{\text{eff}}u}{2D_m} \quad (39)$$

which can be interpreted as the *universal mobile phase velocity* – universal because parameter d_{eff} in it is measured the same way for all columns. Let $v_{U,\text{opt}}$ be v_U at $u = u_{\text{opt}}$. Comparison of Eqs. (36), (37) and (39) yields:

$$v_{U,\text{opt}} = \begin{cases} D_n/D_m, & \text{LC} \\ D_n/D_{m,\text{st}} & \text{GC} \end{cases} \quad (40)$$

indicating that the *optimal universal mobile phase velocity* ($v_{U,\text{opt}}$) of a given solute in a given column is the ratio of its molecular and nominal diffusivities in the column. More experimental data is needed to find out how well a single value of $v_{U,\text{opt}}$ for a column class can represent that class.

Due to carrier gas compressibility in GC, u_{opt} can be different at different locations along a column. This complicates the whole concept of u_{opt} and its measurement in GC. For an ideal gas, the product pu of pressure (p) and u is the same at any location [26, 36, 63]. Thus:

$$pu = p_o u_o, \quad pu_{\text{opt}} = p_o u_{o,\text{opt}}, \quad (\text{ideal gas}) \quad (41)$$

where u_o and $u_{o,\text{opt}}$ are u and u_{opt} at the column outlet. Quantity pu can be further transformed into a measurable volumetric flow rate (F) measured in GC at predetermined pressure (typically 1 atm) and temperature (typically 25 °C) [26, 39, 64]. For a given column:

$$\frac{u}{u_{\text{opt}}} = \frac{F}{F_{\text{opt}}} \quad (42)$$

where F_{opt} is the optimal F corresponding to u_{opt} . Being a function of H , Eq. (29), quantity e_s is a function of u/u_{opt} , i.e. the notation e_s is an abbreviated notation for the functions $e_s(u/u_{\text{opt}})$ and $e_s(F/F_{\text{opt}})$, i.e. $e_s = e_s(u/u_{\text{opt}}) = e_s(F/F_{\text{opt}})$ – the same way as H actually stands for $H(u/u_{\text{opt}})$.

So far, we identified a column intensive properties represented by parameters d_{eff} , e_s and D_n . The extensive properties represented by parameters E , t_M and L of a particular column relate to quantities d_{eff} , e_s and D_n as [15, 39] (Supplement):

$$E = \frac{d_{\text{eff}}}{\sqrt{2D_n j_{\text{st}} t_p}} \left(e_s \sqrt{\frac{F_{\text{opt}}}{F}} \right) \quad (43)$$

$$t_M = \frac{d_{\text{eff}}^4}{4D_n^2 j_{\text{st}}^2 t_p} \left(\frac{F_{\text{opt}}}{F} \right)^2 \quad (44)$$

$$\frac{L}{d_{\text{eff}}^3} = \frac{1}{2D_n j_{\text{st}} t_p} \frac{F_{\text{opt}}}{F} \quad (45)$$

In these expressions:

$$j_{\text{st}} = \begin{cases} 1, & \text{LC} \\ \frac{p_{\text{st}} j}{p_o}, & \text{GC} \end{cases} = \begin{cases} 1, & \text{LC} \\ \frac{3p_{\text{st}}(p_i + p_o)}{2(p_i^2 + p_i p_o + p_o^2)}, & \text{GC} \end{cases} \quad (46)$$

where j is the *James-Martin compressibility factor* [26, 65]. Eqs. (43), (44) and (45) express parameters t_M , E and L of a particular column at a fixed instrumental pressure (represented by parameter t_p) as functions of:

- parameters e_s and D_n of a class of self-similar columns to which the column belongs
- parameter d_{eff} of a particular column
- variable F/F_{opt} – the *relative* flow rate in the column

The remaining parameter, j_{st} in the expressions represents a separation technique (GC with strong or weak gas decompression along the column, or LC with incompressible solvent) rather than operational conditions in a technique.

As e_s is a function of F/F_{opt} , the combination $(e_s \sqrt{F_{\text{opt}}/F})$ in Eq. (43) represents a net functions of F/F_{opt} . The same is true for similar combinations in other equations. When F/F_{opt} is fixed, e_s is fixed even if F and/or F_{opt} vary. Eqs. (43), (44) and (45) allow one to evaluate the effect of parameters d_{eff} , e_s and D_n at a fixed F/F_{opt} (e.g. when $F = F_{\text{opt}}$). Eq. (45) shows that [15, 39]:

In order to keep the ratio F/F_{opt} fixed for all self-similar columns with different effective diameters and lengths operating under the same pressure, the ratio L/d_{eff}^3 must be fixed.

According to Eqs. (43) and (44), the following relations of proportionality for self-similar columns exist:

$$E \sim d_{\text{eff}}, \quad t_M \sim d_{\text{eff}}^4, \quad (\text{fixed } t_p \text{ and } F/F_{\text{opt}}) \quad (47)$$

Also, together with Eqs. (45) and (46), Eqs. (43) and (44) describe the dependencies of E , t_M and L on t_p and, therefore, on the column pressure. In GC with weak gas decompression along a column

423 ($|\Delta p| \ll p_o$) and in LC, quantity j_{st} is fixed ($j_{st} = 1$ in LC, $j_{st} = p_{st}/p_o$ in GC with $|\Delta p| \ll p_o$). As a result,
 424 Eqs. (44), (43) and (45) provide a complete picture of dependencies of E , t_M and L on Δp (t_M and L are
 425 proportional to Δp while E is proportional to $\sqrt{\Delta p}$). This is different in GC with significant gas
 426 decompression along the column where presence of the pressure-dependent parameter j_{st} in Eqs. (43),
 427 (44) and (45) affects these dependencies on Δp . In the extreme case of GC-MS where $p_o = 0$ and
 428 $p_i = \Delta p$, the dependencies become simpler. Eq. (46) yields:

$$429 \quad j_{st} = \frac{3p_{st}}{2\Delta p}, \quad (\text{GC-MS}) \quad (48)$$

430 which, together with Eq. (18) allows one to express Eqs. (43), (44) and (45) as:

$$431 \quad E = \frac{d_{\text{eff}} \Delta p}{\sqrt{96 D_n p_{st} \eta}} \left(e_s \sqrt{\frac{F_{\text{opt}}}{F}} \right), \quad (\text{GC-MS}) \quad (49)$$

$$432 \quad t_M = \frac{d_{\text{eff}}^4 \Delta p^3}{288 D_n^2 p_{st}^2 \eta} \left(\frac{F_{\text{opt}}}{F} \right)^2, \quad (\text{GC-MS}) \quad (50)$$

$$433 \quad \frac{L}{d_{\text{eff}}^3} = \frac{\Delta p^2}{96 D_n p_{st} \eta} \frac{F_{\text{opt}}}{F}, \quad (\text{GC-MS}) \quad (51)$$

434 indicating that, in order to maintain a fixed ratio F/F_{opt} in self-similar columns with the same d_{eff} in
 435 GC-MS, L should increase in proportion to Δp^2 causing an increase in E and t_M in proportion to Δp and
 436 Δp^3 , respectively.

437 Also instructive is the relationship between t_M and E in a column operating below the instrumental
 438 pressure limit where the t_p value is not a consideration. Exclusion of t_p from Eqs. (43) and (44) yields:

$$439 \quad t_M = \frac{E^2 d_{\text{eff}}^2}{2 D_n j_{st}} \left(\frac{F_{\text{opt}}}{e_s^2 F} \right) \quad (52)$$

440 This equation is valid for LC and for GC with any degree of gas decompression along a column.

441 However, similar to Eqs. (43), (44) and (45), quantity j_{st} in Eq. (52) is fixed only in the case of GC

442 with weak gas decompression along a column and in LC. In these cases, Eq. (52) can be expressed as:

$$443 \quad t_M = \frac{E^2 d_{\text{eff}}^2}{2D_n} \left(\frac{F_{\text{opt}}}{e_s^2 F} \right) \cdot \begin{cases} 1, & \text{LC} \\ p_{st}/p_o, & \text{GC at } |\Delta p| \ll p_o \end{cases} \quad (53)$$

444 In GC with significant gas decompression, the presence of the pressure-dependent parameter j_{st} in Eq.

445 (52) complicates the relationship between d_{eff} , E and t_M . The relationship becomes simple in GC-MS.

446 Excluding Δp from Eqs. (49) and (50). One has:

$$447 \quad t_M = d_{\text{eff}} E^3 \sqrt{\frac{32\eta}{3D_n p_{st}}} \left(\frac{1}{e_s^3} \sqrt{\frac{F_{\text{opt}}}{F}} \right), \quad (\text{GC-MS}) \quad (54)$$

448 Eqs. (52), (54), (33) and (51) represent the following relations of proportionality for self-similar

449 columns operating at fixed F/F_{opt} [15, 26, 39, 45, 66]:

$$450 \quad t_M \sim E^2, \quad (\text{fixed } d_{\text{eff}} \text{ in GC at } \Delta p \ll p_o \text{ and in LC at } \Delta p < \Delta p_{\text{max}}) \quad (55)$$

$$451 \quad t_M \sim E^3, \quad (\text{fixed } d_{\text{eff}} \text{ in GC at } p_o \ll \Delta p < \Delta p_{\text{max}}) \quad (56)$$

$$452 \quad t_M \sim E^4 \quad (\text{fixed } \Delta p \text{ and } \eta) \quad (57)$$

453 indicating that, if the ratio F/F_{opt} does not change, then the time “price” for increasing the separation

454 performance is the lowest in a column operating below instrumental pressure limit (Δp_{max}) if, on top of

455 that, the gas decompression in GC column is weak ($\Delta p \ll p_o$). On the other hand, the “price” for the

456 separation performance is the highest in a column operating at $\Delta p = \Delta p_{\text{max}}$. Thus, doubling E requires 4

457 times longer t_M in the least “expensive” case, and 16 times longer t_M in the most “expensive” one. In

458 the intermediate case of GC-MS operating below Δp_{max} , doubling E requires 8 times longer t_M .

459 From Eqs. (49), (50) and (51), one can also obtain complete dependencies $t_M(L)$ and $E(L)$

460 (Supplement) not considered here.

461 The analysis developed here suggests that there are two essential differences between transport
462 properties of GC and LC, and between kinetics of the techniques in general.

- 463 • The mobile phase is compressible in GC and essentially incompressible in LC. This difference
464 leads to the unique for GC third power dependence, $t_M \sim E^3$, Eq. (56), of t_M on E , and more
465 generally, to the third power dependence of analysis time on column separation performance.
- 466 • Molecular diffusivity (D_m) in LC is several orders of magnitude lower than that in GC. It follows
467 from Eq. (44) where the product $D_n j_{st}$ is of the same order of magnitude as D_m that, in order to
468 maintain equal t_M (and, therefore, comparable analysis times) in both techniques, d_{eff} in LC should
469 be substantially smaller than that in GC which causes substantially smaller loadability of an OTC
470 LC column compared to that in GC. This, in turn, is the key reason for using the *multi-path*
471 (packed, monolithic, pillar-array, etc.) columns in LC with all consequences of such columns.

472 Other differences between transport properties of the two techniques are less consequential. For,
473 example, liquids have much higher viscosity compared to gases. However, liquids can also sustain
474 much higher pressure than gases. As shown in the comments to Eq. (18), the time-equivalents (t_p), Eq.
475 (18), of the two factors are comparable in both techniques causing no significant external difference in
476 their performance.

477 3. Discussion

478 The forthcoming discussion demonstrates how the metric e_s affects the separation-time tradeoff, and
479 how all three core metrics (e_s , D_n and d_{eff}) can be used for choosing a suitable column and its
480 optimization.

481 The key feature of metrics in this report is that they can be measured experimentally. However, their
482 numerical values in the discussion are based in several cases on theoretical evaluations. It is assumed

483 in all numerical examples and illustrations that a WCOT column has **thin** stationary phase film (film
484 thickness has negligible effect on plate height), and a packed column is packed with **spherical**
485 **particles of the same size**. Parameters of several column types and/or specific columns together with
486 their operational conditions are compiled in **Error! Reference source not found.**

487 Quantity H_{\min} and related parameters in **Error! Reference source not found.** substantially depend
488 on retention factor (k). In **Error! Reference source not found.**, the entries for WCOT columns
489 correspond to $k = 0$ and $k = 2$. The choice of $k = 2$ is not accidental and can be recommended for
490 column comparison. In temperature-programmed GC at optimal heating rate [13, 39, 44], and in
491 gradient LC with optimal mixing rate [15, 17, 45, 66], all solutes elute with $k \approx 2$. As a result,
492 parameters statically measured at $k \approx 2$ also represent elution parameters in optimal dynamic analyses.
493 The k -values for other columns in **Error! Reference source not found.** were taken from published
494 experimental results. The data available for k closest to $k \approx 2$ were chosen where possible. The
495 relationships between t_M and E , Eq. (33), for the data with $k > 0$ in **Error! Reference source not**
496 **found.** are illustrated in Figure 1.

497 3.1 Attainable column performance

498 Eq. (33) and Figure 1 describe and illustrate the dependence of relationship between E and t_M on e_s .
499 However, they don't say what actual E or t_M can be obtained from actually available columns. These
500 values can be found for LC and GC under all operational conditions from Eqs. (43) and (44) which, for
501 specifics of GC-MS were reduced to Eqs. (49) and (50). The optimal values E_{Opt} , $t_{M,\text{Opt}}$ and $e_{s,\text{max}}$ of
502 quantities E , t_M and e_s for the column with $k > 0$ in **Error! Reference source not found.** are compiled
503 in **Error! Reference source not found.**

504 Speaking of attainable performance, we do not attempt to identify specific performance limits for
505 practically available columns of each evaluated type. Instead, we consider this discussion as an

506 illustration of how these issues can be addressed using parameters e_s , D_n and d_{eff} . For that purpose, we
 507 treat the column cross-sectional dimensions in **Error! Reference source not found.** and **Error!**
 508 **Reference source not found.** as the smallest that can be currently manufactured and assume that
 509 larger dimensions are available. The dependencies of E_{Opt} and $t_{\text{M,Opt}}$ on d_{eff} are shown in Figure 2
 510 where the markers correspond to d_{eff} -values in **Error! Reference source not found.**. The thinner lines
 511 to the left of the markers represent the operations that are assumed to be currently impossible as they
 512 require smaller than currently available d_{eff} .

513 Suppose that, in analyses of small molecules, t_{M} larger than 10 min (about 1 hour long analysis at
 514 optimal mixing rate [15, 45, 66]) are unacceptable. Figure 2b and the listing of $t_{\text{M,Opt}}$ (the shortest t_{M}
 515 for a given E in each column type) in **Error! Reference source not found.** show that only GC-MS
 516 WCOT and LC packed columns satisfy this requirement. Interestingly, the two packed columns (the
 517 only two practically useful LC columns at $\Delta p = 1200$ bars) have the lowest (the worse) $e_{\text{s,max}}$ (**Error!**
 518 **Reference source not found.** and **Error! Reference source not found.**) of all columns in **Error!**
 519 **Reference source not found.** and **Error! Reference source not found.**. This is not a contradiction
 520 because $e_{\text{s,max}}$ is a metric of the tradeoff between E and t_{M} for a given *column type*, but not a measure
 521 of E and t_{M} actually obtainable from a *particular column*.

522 The effective diameters found by solving Eqs. (44) and (50) for d_{eff} at $t_{\text{M}} = 10$ min and $F = F_{\text{opt}}$, as
 523 well as other cross-sectional dimensions of the column types in **Error! Reference source not found.**
 524 that yield $t_{\text{M,Opt}} = 10$ min are listed in **Error! Reference source not found.** together with
 525 corresponding E_{Op} . Also listed in **Error! Reference source not found.** are $e_{\text{s,max}}$ for each column type
 526 (copied from **Error! Reference source not found.**). Using the data in **Error! Reference source not**
 527 **found.**, one can observe that, since all columns yield the same $t_{\text{M,Opt}}$, a column with larger $e_{\text{s,max}}$ yields

528 proportionally larger E_{Opt} . And, of course, as their $e_{s,\text{max}}$ are the lowest, the two packed LC columns
529 have the lowest E_{Opt} .

530 The data in **Error! Reference source not found.** also show that, in order to yield a reasonable void
531 time at high Δp (10 min and 1200 bar in **Error! Reference source not found.**), the d_{eff} of a LC
532 column should be in vicinity of 1 μm , and internal diameters (d) of an OTC (WCOT, PLOT) in LC
533 should be close to that. With so small internal diameter, a reasonably fast LC OTC has very low
534 *loadability*. For that reason, no LC OTC is included in further evaluations. Also excluded are the
535 WCOT GC columns typical for GC. Their separation-time tradeoffs are practically limited not by the
536 maximum available pressure, but by the loadability [39].

537 Among the remaining pillar-array and conventional packed columns (core-shell and totally porous),
538 the pillar-array ones ($e_{s,\text{max}} = 0.643$) appear to have 56% to 93% better transport quality compared to
539 the packed columns ($e_{s,\text{max}} = 0$.**Error! Reference source not found.** and **Error! Reference source not**
540 **found.**). Thus, the pillar-array column in **Error! Reference source not found.** delivers 56% to 93%
541 larger E , respectively, than the other two deliver with the same $t_{\text{M,Opt}}$. However, in order to realize their
542 structural advantage and obtain their higher available E in a practically reasonable $t_{\text{M,Opt}}$, the pillar
543 dimensions should be reduced by about a factor of 2 – from the ones in **Error! Reference source not**
544 **found.** to those in **Error! Reference source not found.**. Without that, the pillar-array columns can
545 compete with conventional packed ones only in the instruments that cannot supply high pressure.

546 3.2 Sub-optimal LC operations

547 So far, the changes in column dimensions were evaluated at fixed ratio F/F_{opt} with possible changes
548 in F and F_{opt} . The fixed F/F_{opt} case includes the *flow-optimized* case of $F = F_{\text{opt}}$. As shown below,
549 allowing for the ratio F/F_{opt} to change and for the column to operate at sub-optimal conditions
550 ($F \neq F_{\text{opt}}$) can be beneficial in some cases.

551 Let E_{Opt} and $t_{\text{M,Opt}}$ be the transport efficiency and the void time, respectively, in a column having
 552 effective diameter d_{eff} and flow-optimized at the instrumental pressure limit (Δp_{max}). Suppose that E_{Opt}
 553 is substantially different from a required *target* E (E_{targ}). Three ways of obtaining E_{targ} are considered
 554 below.

555 (a) Ideally, one would prefer another self-similar column, the *target* one, that has its own effective
 556 diameter $d_{\text{eff,targ}}$ and optimal flow ($F_{\text{opt,targ}}$) so that, at $F = F_{\text{opt,targ}}$ and Δp_{max} , its optimal E is E_{targ} .

557 Due to proportionality $E \sim d_{\text{eff}}$, Eq. (47), one has:

$$558 \quad \frac{d_{\text{eff,targ}}}{d_{\text{eff}}} = \frac{E_{\text{targ}}}{E_{\text{Opt}}} \quad (58)$$

559 (b) If $E_{\text{targ}} < E_{\text{Opt}}$ then E_{targ} can be obtained at $F = F_{\text{opt}}$ and $\Delta p < \Delta p_{\text{max}}$ in a shorter column.

560 (c) E_{targ} can be also obtained at Δp_{max} by changing the column length (L) without changing d_{eff} [11,
 561 14, 58] and allowing for $F \neq F_{\text{opt}}$.

562 Different conditions lead to different t_{M} , Figure 3, at the same E_{targ} . It follows from Eqs. (55) and
 563 (57) that the ratio $t_{\text{M}}/t_{\text{M,Opt}}$ is proportional to $(E_{\text{targ}}/E_{\text{Opt}})^4$ in case (a) and to $(E_{\text{targ}}/E_{\text{Opt}})^2$ in case (b). The
 564 relations in case (c) are more complex and depend on specifics of dependency of H (and, therefore, e_s)
 565 on F/F_{opt} . Shown in Figure 3 are the graphs based on Eq. (34) with several values of parameter a
 566 defined in Eq. (34). The mathematics are described in the Supplement.

567 Figure 3 confirms that, as expected, the target column having effective diameter $d_{\text{eff,targ}}$ and operating
 568 at $F = F_{\text{opt,targ}}$, case (a), provides the most *time-efficient* way of obtaining E_{targ} , i.e. the shortest t_{M} at
 569 E_{targ} regardless of the difference between E_{targ} and E_{Opt} , or, from another perspective [58], regardless of
 570 the difference between the required effective diameter ($d_{\text{eff,targ}}$) and the available one (d_{eff}). Suppose
 571 that $E_{\text{targ}} < E_{\text{Opt}}$, but d_{eff} cannot be reduced. The time saving due to reduction in E without changing d_{eff}
 572 can be obtained by reducing the column length (L). Two ways of doing so are illustrated in Figure 3. In

case (b), a shorter column can be flow-optimized at $\Delta p < \Delta p_{\max}$. In case (c), the column length is reduced without reducing Δp , i.e. keeping $\Delta p = \Delta p_{\max}$ and, therefore, using non-optimal flow $F > F_{\text{opt}}$. Figure 3 shows that (b) is the least time-efficient case – it requires the longest t_M for obtaining the same E_{targ} . One can conclude that,

The most time-efficient way of obtaining a required E (E_{targ}) is by using a target column having target effective diameter ($d_{\text{eff,targ}}$) that optimizes the column at maximum instrumental pressure (Δp_{\max}). However, if $E_{\text{targ}} < E_{\text{Opt}}$ but a column with smaller d_{eff} is not available, it is always more time-efficient to obtain E_{targ} at Δp_{\max} using non-optimal flow rather than using optimal flow at $\Delta p < \Delta p_{\max}$.

Figure 3 at $E_{\text{targ}}/E_{\text{Opt}} > 1$ also shows that it is possible to raise E above E_{Opt} by using sub-optimal conditions ($L > L_{\text{Opt}}$ and, therefore, $F < F_{\text{opt}}$) in a column with a given d_{eff} operating at Δp_{\max} , case (c). However, although it is a possibility, this way of raising E is less time-efficient than the case (a) and its highest available E is limited. As shown in the Supplement, in a column with H in Eq. (34), E at Δp_{\max} cannot exceed $\sqrt{2/(1-a)}E_{\text{Opt}}$.

Figure 3 also shows that the purpose of reducing a column characteristic cross-sectional dimensions (d_{eff} , d_p , etc.) without changing Δp is to *reduce the efficiency* with the purpose of disproportionately greater reduction in analysis time.

4. Conclusions

Three measurable parameters (metrics) – effective diameter (d_{eff}), specific efficiency (e_s) and nominal diffusivity (D_n), representing three core intensive properties of GC and LC columns – are

594 sufficient for objective comparison of the column separation-time performance. Quantities e_s and D_n
595 represent the properties of classes of self-similar columns while d_{eff} represent a particular column. The
596 largest number of peaks that a chromatographic system can resolve in a fixed time is proportional to e_s
597 giving rise to interpreting e_s as a measure of column transport quality, or more precisely as the ability
598 of a particular column design to transport and elute the solutes with a minimum of peak broadening
599 and pressure losses. The higher is e_s the shorter (the better) is the analysis time required for resolving
600 the same number of peaks. Quantity e_s is equivalent to, introduced here, universal plate height (h_U) and
601 to separation impedance (SI) introduced by Bristow and Knox for packed LC columns and extended
602 here to all LC and GC columns. All three (e_s , h_U and SI) are nothing but differently normalized and
603 differently powered familiar dimensionless plate heights. The advantage of the quantity e_s over the
604 others is that it is proportional to the number of components that can be resolved with a given column
605 which is the ultimate performance measure for any chromatographic column.

606 The time of chromatographic analysis is proportional to void time (t_M) while the largest number of
607 peaks that a column can resolve is proportional to the column transport efficiency (E) which, in turn, is
608 proportional to e_s . It has been shown that the core set of parameters (d_{eff} , e_s and D_n) is sufficient for
609 describing the relations between E , t_M and other specific parameters of a column and its operation
610 (column length (L), flow rate (F), pressure drop (Δp), etc.). The relationships between d_{eff} , e_s and D_n on
611 the one hand and parameters E , t_M , Δp , L and F on the other have been established. Some implications
612 of these relations are:

613 In a column operating below instrumental pressure limit, reduction in d_{eff} can be used for making
614 larger E , or shorter t_M , or for obtaining both improvements. Reducing d_{eff} increases required Δp . Once
615 the instrumental pressure limit is reached, the effect of further reduction in d_{eff} changes. If a fixed ratio

616 F/F_{opt} is maintained at any d_{eff} and fixed Δp then the reduction in d_{eff} reduces t_M in proportion with the
617 4th power of reduction in d_{eff} at the expense of reducing E in proportion with the reduction in d_{eff}

618 To keep the ratio F/F_{opt} fixed when d_{eff} changes and Δp does not, the change should be accompanied
619 by changing L in a way that keeps the ratio L/d_{eff}^3 fixed.

620 The most time-efficient way of obtaining a required (target) E (E_{targ}) is by using a target column
621 having target effective diameter ($d_{\text{eff,targ}}$) that optimizes the column at maximum instrumental pressure
622 (Δp_{max}). However, even if a column with $d_{\text{eff,targ}}$ is not available, it is always more time-efficient to
623 obtain E_{targ} at Δp_{max} using sub-optimal conditions rather than using optimal conditions at $\Delta p < \Delta p_{\text{max}}$.

624 Although only LC and GC are considered, the study in this report suggests that the same approach
625 can be extended to other techniques where the concepts similar to those of void time and maximum
626 available pressure can be identified.

627 **5. Nomenclature**

628 **Abbreviations:**

629 OTC – open-tubular column

630 PLOT – porous layer open tubular

631 SI – separation impedance

632 SPI –specific performance index

633 WCOT – wall-coated open-tubular

634 **Subscripts:**

635 max – maximum

636 min – minimum

- 637 opt – optimum at H_{\min}
- 638 Opt – optimum at lowest H_{\min} and fixed Δp

Symbol	Description
d	internal diameter of open space in OTC
d_c	internal diameter of column tubing
d_{eff}	effective diameter, Eq. (16)
d_p	particle size
D_m	solute diffusivity in mobile phase
$D_{m,\text{st}}$	D_m at 1 atm
D_n	nominal diffusivity, Eq. (37)
D_{np}	D_n rescaled to pressure p , Eq. (36)
E	transport efficiency, Eq. (5)
e_s	specific transport efficiency, Eq. (29)
F	mobile phase volumetric flow rate
H	(apparent) plate height, Eqs. (2) and (6)
h	dimensionless plate height, Eqs. (3) and (4)
h_U	universal plate height, Eq. (25)
j_H	Halász-Hartmann-Heine compressibility factor, Eq. (10)
j_{st}	Eq. (46)
k	retention factor (the same as k')
K_v	transport permeability, Eq. (8)
L	column length
m	statistically expected number of resolved peaks
n_c	peak capacity
p	pressure
p_i	inlet pressure
p_o	outlet pressure
p_{st}	standard pressure, $p_{\text{st}} = 1$ atm
Δp	pressure drop
Δp_{eff}	effective pressure, Eq. (9)
s	separation capacity
t	time

t_M	void time
t_p	time-equivalent of pressure and viscosity, Eq. (18)
u	mobile phase velocity
u_o	mobile phase outlet velocity
η	mobile phase viscosity
σ	peak standard deviation (width)
ϕ	transport resistance factor, Eq. (13)

640 **6. References**

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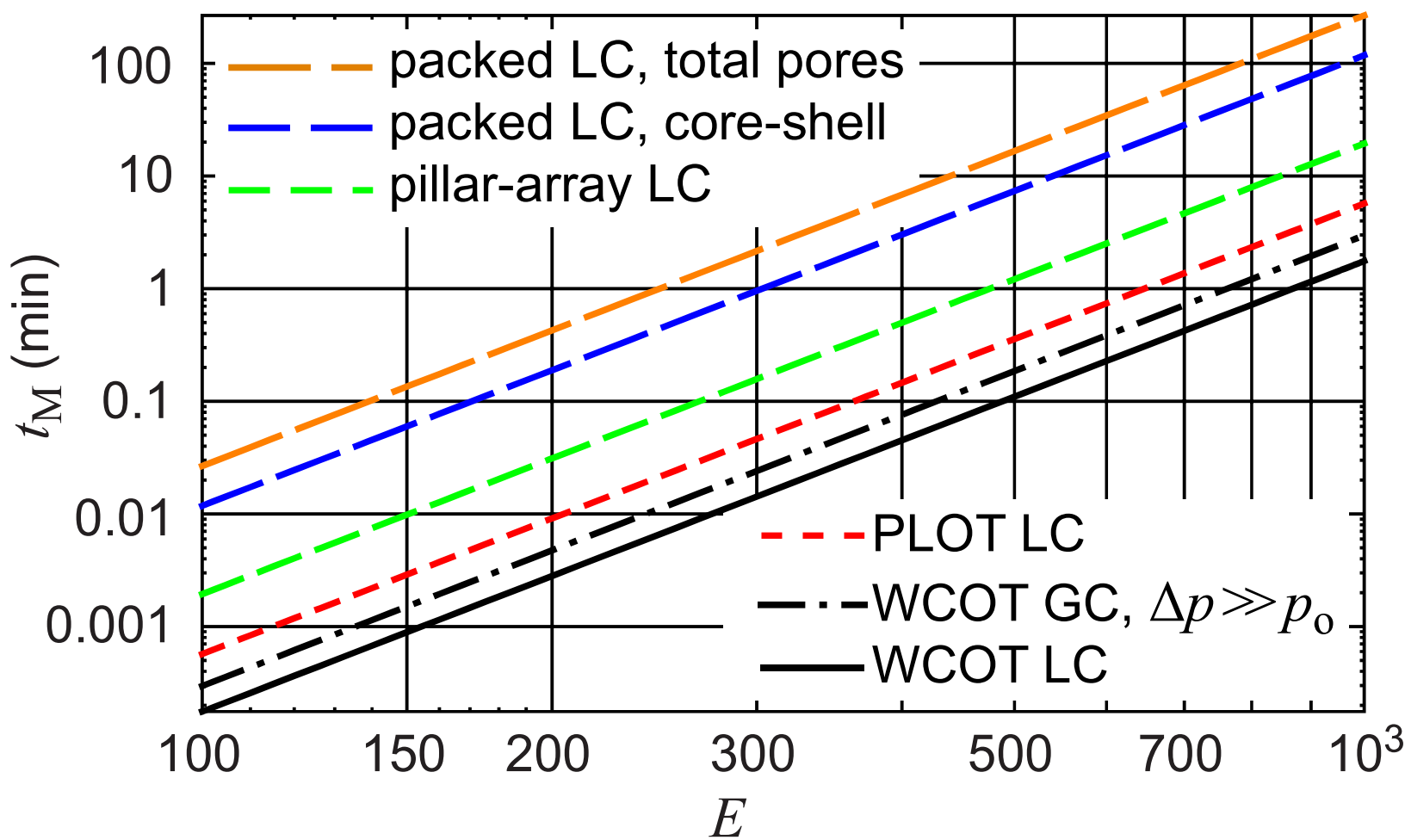
795 **Figure Captions**

796 Figure 1. Void time (t_M) vs. efficiency (E), Eq. (33), at maximum specific efficiency ($e_{s,max}$), Table 1,
797 for each column type operating at $t_p = 0.2$ ns – nearly the lowest (the best) practical t_p , Eq. (19). In each
798 column type, E at the same t_M is proportional to its $e_{s,max}$, while t_M at a the same E is inversely
799 proportional to $e_{s,max}^4$.

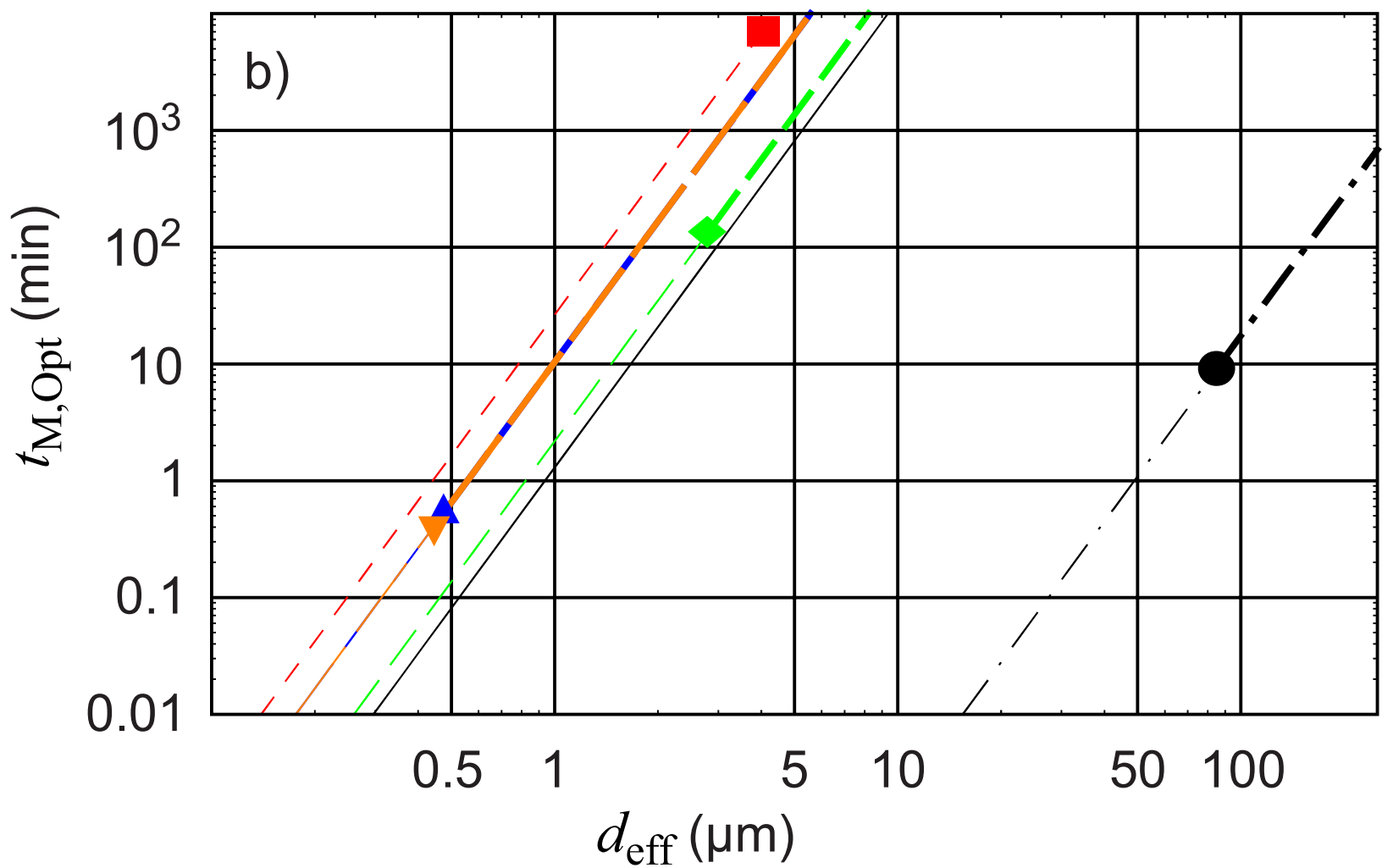
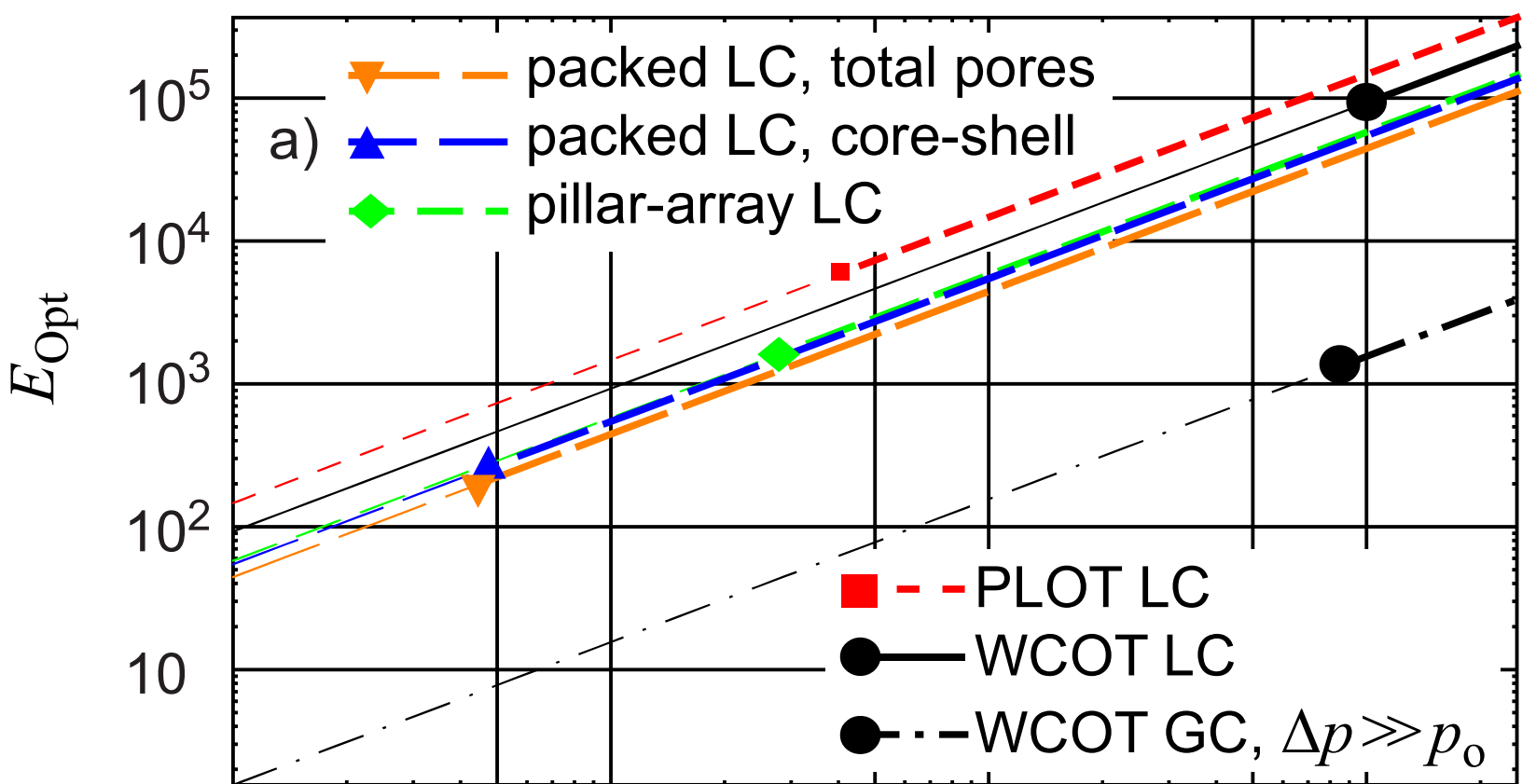
800 Figure 2. Optimal transport efficiency and void time (E_{Opt} and $t_{M,Opt}$), Eqs. (43), (44), (49) and (50), vs.
801 effective diameters (d_{eff}) in Table 2 for the columns operating at $t_p = 0.2$ ns. All other conventions and
802 conditions are the same as in Figure 1. The $t_{M,Opt}$ marker for LC WCOT in (b) falls far above the graph.

803 Figure 3. Void time (t_M) at the same target efficiency (E_{targ}) in several columns and conditions as
804 explained in the main text. Due to Eq. (58), the graphs can be interpreted as functions of the ratio
805 E_{targ}/E_{Opt} or [58] of the ratio $d_{eff,targ}/d_{eff}$. The dash-dot line for $\Delta p \leq \Delta p_{max}$, case (b), only exists at
806 $E_{targ} \leq E_{Opt}$, i.e., equivalently, at $d_{eff,targ} \leq d_{eff}$.

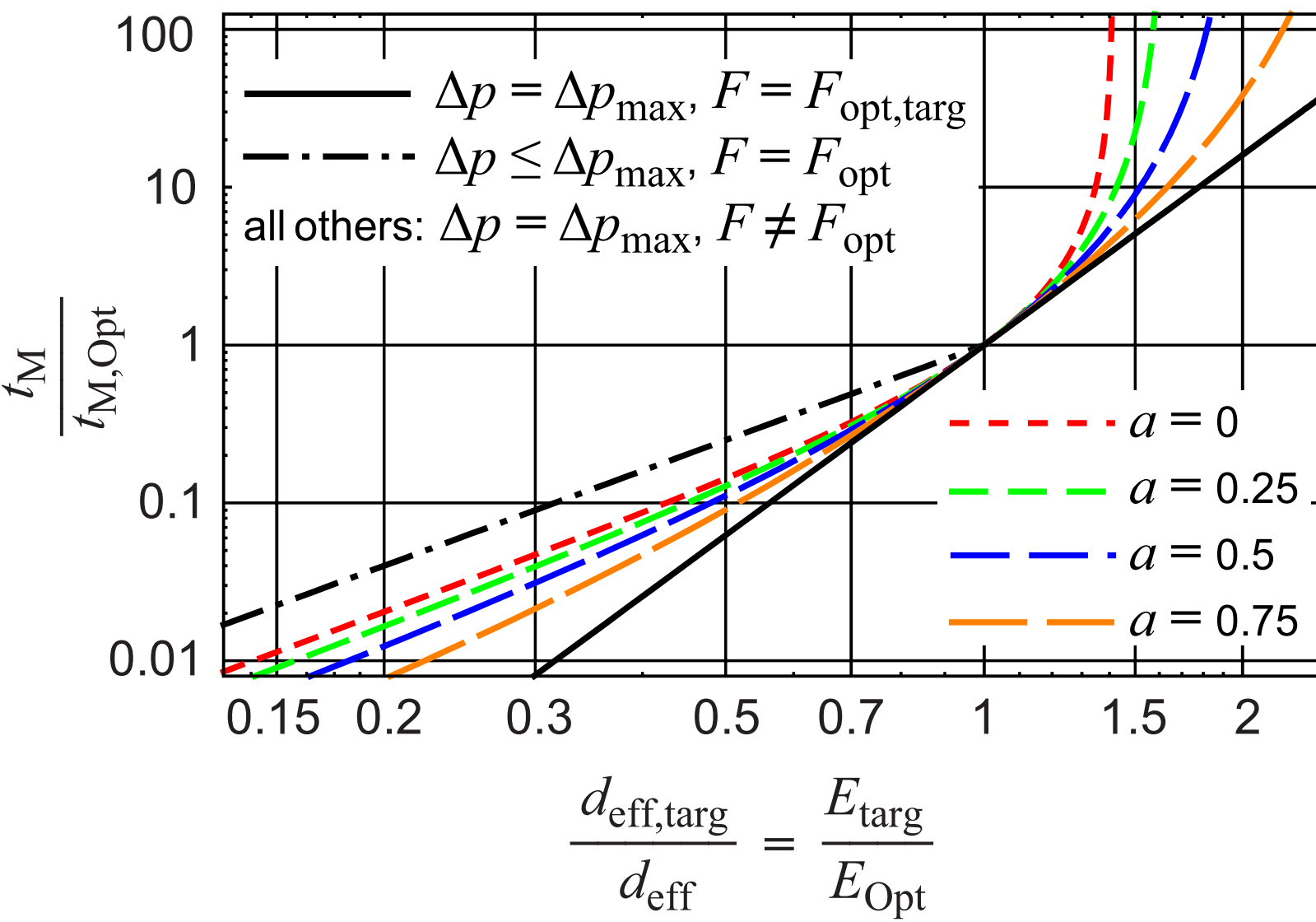
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Figure



Tables

Table 1. Column parameters and experimental conditions.

Column	Conditions		K_v	d_{eff} Eq. (17)	H_{min}	$e_{\text{s,max}}$ Eq. (29)	$h_{\text{U,min}}$ Eq. (25)	SI_{min} Eq. (24)	
WCOT [26]	$k = 0$	GC at $ \Delta p \ll p_o$, LC	$d^2/32$	d	$0.289d$	1.861	0.289	2.67	
		GC-MS		$0.866d$	$0.325d$	1.633	0.375	4.5	
	$k = 2$	GC at $ \Delta p \ll p_o$, LC		d	$0.726d$	1.173	0.726	16.9	
		GC-MS		$0.866d$	$0.817d$	1.029	0.944	28.5	
PLOT [67]	LC	$k = 1.42$		$d^2/39.2$	$0.903d$	$5.24 \mu\text{m}$	0.874	1.31	54.7
Pillar-array [21]		$k = 2.3$		$0.27 \mu\text{m}^2$	$2.94 \mu\text{m}$	$7.1 \mu\text{m}$	0.643	2.41	186
Packed CS [68]		$k = 6$	$\varphi_p = 1/6$	$d_p^2/569$	$0.237d_p$	$1.4d_p$	0.412.	5.9	1115
Packed TP [68]		$\varepsilon_p = 0.4$	$\varphi_p = 1/2$	$d_p^2/640$	$0.224d_p$	$2d_p$	0.334	8.94	2560

Notes:

The columns are listed in the order of decreasing (worsening) $e_{\text{s,max}}$.

Quantities H_{min} , $e_{\text{s,max}}$, $h_{\text{U,min}}$ and SI_{min} are H , e_s , h_U and SI , respectively, at $F = F_{\text{opt}}$.

Highlighted are only the values of $e_{\text{s,max}}$ at $k > 0$.

CS = core-shell, TP = total porosity, ε_p = porosity of packing material, $\varphi_p = d_s/d_p$ (d_s = shell thickness).

Table 2. Performance (E_{Opt} , $t_{\text{M,Opt}}$) of several column types at $t_p = \eta/\Delta p = 0.2$ ns, Eq. (19).

Technique	Column	$D_n/(\text{cm}^2/\text{s})$, source	d_{cx}	$d_{\text{cx}}/\mu\text{m}$	$d_{\text{eff}}/\mu\text{m}$	$e_{\text{s,max}}$	E_{Opt} , Eqs. (44), (50)	$t_{\text{M,Opt}}/\text{min}$, Eqs. (45), (51)
GC-MS	WCOT	1.3, Eq. (38)	d	100	86.6	1.029	1349	9.83
LC	WCOT	0.00004, estimate	d	100	100	1.173	92726	1.3×10^8
	PLOT [67]	0.0000088	d	4.59	4.15	0.874	6084	7813
	Pillar-array [21]	0.000031	$(d_{\text{pil}}, \Delta y)$	(5, 2.5)	2.94	0.643	1702	163
	packed CS	0.000014, Eq. (38)	d_p	2	0.474	0.412	260	0.527
	packed TP	0.000014, Eq. (38)	d_p	2	0.447	0.334	199	0.417

Notes:

D_n values in LC represent small molecules only.

d_{pil} and Δy are pillar diameter and inter-pillar distance, respectively [21].

d_{cx} is a symbol for cross-sectional dimensions d , d_{pil} , Δy , d_p of different columns

Other conventions are as in Table 1

Table 3. Cross-sectional dimensions (d_{eff} , d_{cx}) and optimal efficiency (E_{Opt}) for the columns in Table 2 at $t_p = \eta/\Delta p = 0.2$ ns and $t_{\text{M,Opt}} = 10$ min.

Technique	Column	d_{cx}	$d_{\text{cx}}/\mu\text{m}$	$d_{\text{eff}}/\mu\text{m}$ Eqs. (45), (51)	$e_{\text{s,max}}$	E_{Opt} Eqs. (44), (50)
GC-MS	WCOT	d	100.4	87	1.029	1355
LC	WCOT	d	1.67	1.67	1.173	1544
	PLOT	d	0.868	0.784	0.874	1151
	Pillar	$(d_{\text{pil}}, \Delta y)$	(2.49, 1.24)	1.46	0.643	847
	packed CS	d_p	4.17	0.99	0.412.	541
	packed TP	d_p	4.43	0.99	0.334	440

Notes: d_{cx} values were found by rescaling their counterparts in Table 2 in proportion with changes in their d_{eff} values.

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