

Review

# Mechanistic molecular model of liquid–solid chromatography Retention–eluent composition relationships

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## Abstract

The development of a simple molecular model of liquid–solid chromatography leading to linear logarithmic relationships between retention factor and eluent composition is discussed. Further evolution of the model and its practical applications in method development are reviewed.

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## Contents

|                                 |     |
|---------------------------------|-----|
| 1. Introduction .....           | 109 |
| 2. Liquid–liquid systems .....  | 109 |
| 3. Liquid–solid systems .....   | 112 |
| 4. Reversed-phase systems ..... | 114 |
| 5. Conclusions .....            | 115 |
| References .....                | 115 |

## 1. Introduction

Earlier theories of method development in chromatography recommended the use of eluotropic series containing even several tens of solvents to choose solvents securing moderate retention of solutes to be separated; however, it was soon realised that mixtures of few solvents are sufficient to control retention. Moreover, by mixing various solvents eluent binaries of similar retention but different selectivities (isoelectropic series) can be obtained [1–3].

## 2. Liquid–liquid systems

In 1960, during a 3-month visit to the Institute of Organic Chemistry and Biochemistry of Stockholm University (chairman Prof. Dr. Carl Axel Wachtmeister) I became interested in the effect of solvent composition on retention in liquid–liquid partition chromatography. In cooperation with Prof. Wachtmeister we published a paper on the quantitative retention vs. stationary phase composition relationships of four dihydroxydibenzofurans (Fig. 1); we demonstrated that  $R_M$  values (log  $k$  values) of the

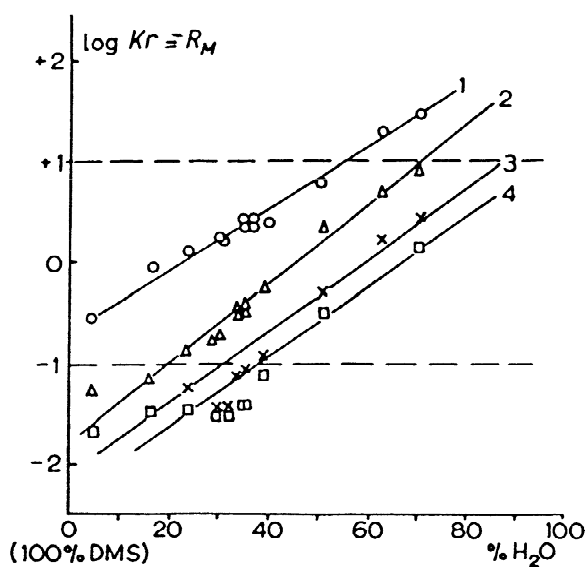


Fig. 1.  $R_M$  values of dihydroxydibenzofurans plotted against %H<sub>2</sub>O for the system: paper+dimethylsulfoxide+water/di-*n*-butyl ether [4].

solutes are linearly dependent on the volume composition of the mixed stationary phase composed of water and dimethylsulfoxide (DMSO) [4]:

$$R_m = \varphi_1 R_{M_w} + \varphi_2 R_{M_{(DMSO)}} \quad (1)$$

or

$$\log k = \varphi_1 \log k_w + \varphi_2 \log k_{DMSO} \quad (1a)$$

Eq. (1) is a modification of an equation for batch liquid–liquid systems in which the components 1,2 of binary mixed phase are immiscible with the second phase [5].

The semilogarithmic relationship Eq. (1a) was found to be valid for some partition systems, e.g., heptane+benzene/water; however, for solvent binaries composed of a polar solvent (modifier) and a non-polar solvent (diluent) strong deviations from linearity were observed, e.g., for phenolic acids chromatographed in the system cyclohexane+tributyl phosphate (TBP)/cellulose+water (Fig. 2). The interpretation of this phenomenon was found by analogy to extraction of metal ions by TBP [6] according to the reaction:

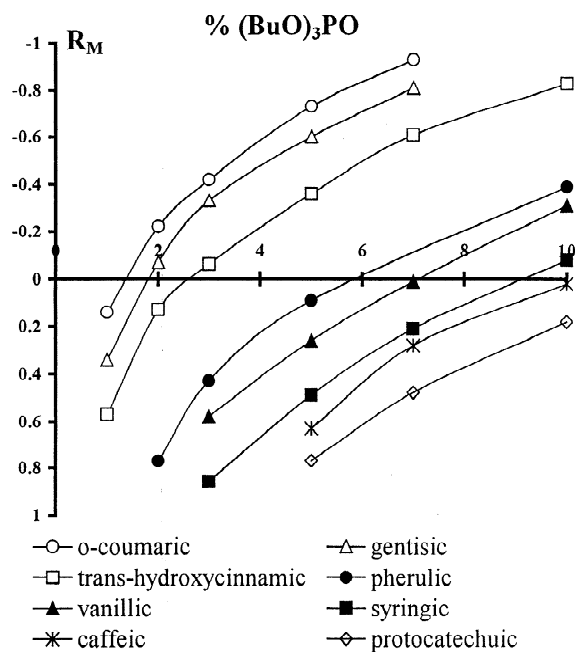
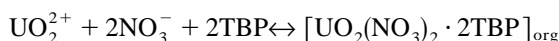


Fig. 2.  $R_M$  values of phenolic acids plotted against volume per cent content of tributyl phosphate in cyclohexane (semilogarithmic system of coordinates,  $R_M = \log k$ ).



The extraction constant for two-phase reaction is then:

$$E = \frac{[UO_2(NO_3)_2 \cdot 2TBP]_{org}}{[UO_2^{2+}][NO_3^-]^2[TBP]^2}$$

and the distribution ratio:

$$D = \frac{C_{org}}{C_w} = \frac{[UO_2(NO_3)_2 \cdot 2TBP]_{org}}{[UO_2^{2+}]} \\ = E [NO_3^-]^2 [TBP]^2 = \text{const} [TBP]^2$$

$$\log D = \text{const} + 2 \log [TBP] \quad (2)$$

The linear log–log relationships were confirmed experimentally (Fig. 3).

We applied this reasoning to partition chromatography of phenolic acids, assuming that they can form solvation complexes with TBP or other H-bonding modifiers according to the reaction:

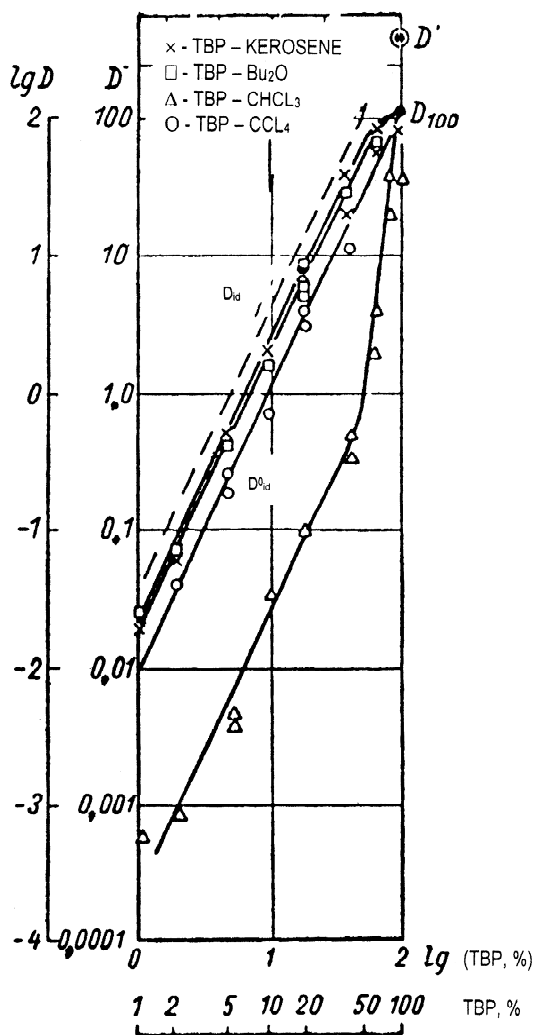
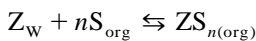


Fig. 3. Log  $D$  values of uranyl nitrate plotted against per cent concentration of tributyl phosphate in various diluents (log–log plot) [6].



where  $Z$  — solute,  $S$  — modifier

$$E = \frac{[ZS_n]_{org}}{[Z]_w \cdot [S]_{org}^n}$$

$$D = \frac{[ZS_n]_{org}}{[Z]_w} = E[S]^n$$

$$\text{Log } D = \text{const} + n \log [S]$$

(3)

For normal-phase system:

$$-R_M = -\log k = \log D \frac{V_{org}}{V_w}$$

therefore,

$$-R_M = \text{const} + n \log [S] \quad (3a)$$

In fact, the plots were found to be linear in the log–log co-ordinate system [7] (Fig. 4).

The linear logarithmic relationship was confirmed for numerous solutes and modifiers; in wider concentrations ranges of modifier the solvation number  $n$  decreases for lower  $[S]$  values in accordance with the shifting solvation equilibrium but for a narrow concentration range usually one type of solvate predominates. Formation of internal H-bond (e.g., for vicinal hydroxyl groups in the solute molecule) causes that the slope  $n$  is diminished [8,9]; for polyfunctional solutes it may be impossible for steric

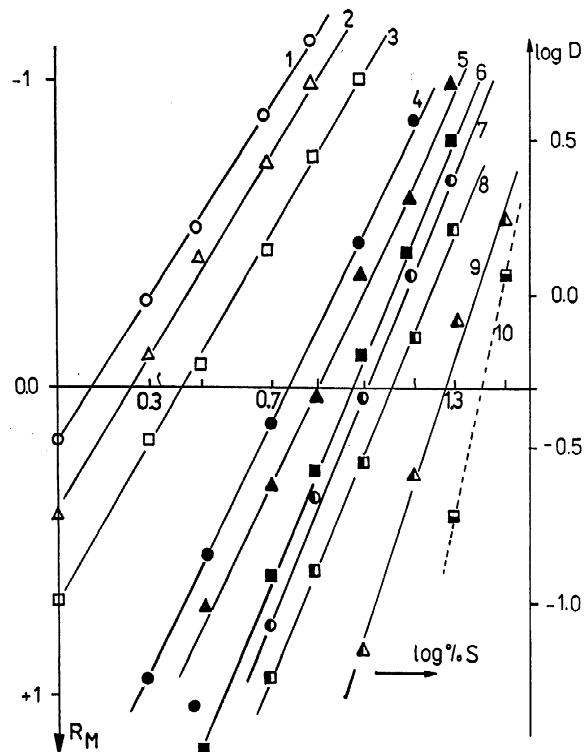


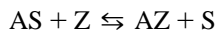
Fig. 4. Data of Fig. 2 plotted in log–log coordinate system [7].

reasons to solvate all H-bonding groups so that the slope is lower than the number of groups.

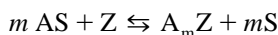
### 3. Liquid–solid systems

Investigations of other retention mechanism demonstrated that for gas–liquid partition systems with binary, liquid stationary phase Eq. (1a) is valid [10], however, for liquid–solid adsorption systems strong deviations from linearity was observed for the semilogarithmic plot (Fig. 5a [11]) but were linear in the log–log plot (Fig. 5b). By analogy to Figs. 3 and 4 I came to the conclusion that also in this case defined molecular complexes are formed in accordance with the law of mass action, this time with surface silanol groups of silica. Somewhat earlier Snyder [12] published his competitive adsorption model in which it was assumed that adsorbent surface is covered with adsorbed layer of solvent molecules and adsorption of a solute molecule must be accompanied by desorption of one or more solvent molecules from the surface. Combining this concept with my earlier experience I formulated a simple molecular model of adsorption from solutions, analogous to ion-exchange equilibria except that formation of ion pairs was replaced by H-

bonding. For monofunctional solute Z adsorption was considered as formation of molecular complex (AZ) with a silanol group (A) with release of a modifier molecule (S) (Fig. 6a):



In accordance with Snyder's model of competitive adsorption, the surface silanol groups (A) are covered with H-bonded molecules of the polar component of the eluent (S). The adsorption of solute molecule (Z) is accompanied with displacement of a modifier molecule in a reversible reaction. For  $m$ -point adsorption (for solute molecule containing  $m$  polar groups capable of simultaneous interaction with surface silanol groups):



$$k = \frac{X_{A_m Z} \cdot X_S^m}{X_{AS}^m \cdot X_Z}$$

$$k = \frac{X_{A_m Z}}{X_Z} = \frac{\text{const}}{X_S^m}$$

$$R_M = \log k = \text{const} - m \log X_S \quad (4)$$

For monofunctional solute  $m=1$ . However, the slope may be different when H-bonding group is

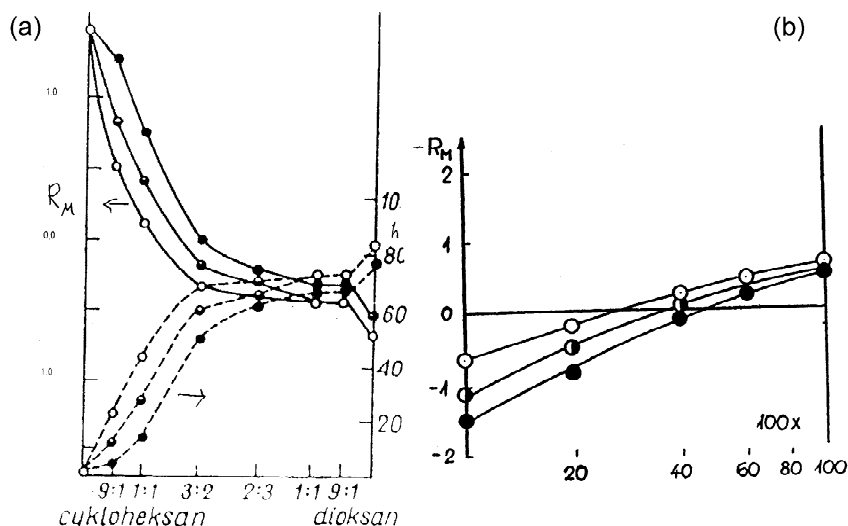


Fig. 5.  $R_M$  values of nitroanilines in the system cyclohexane+dioxane/silica. (a) Semilogarithmic plot ( $R_M$ ,  $R_F$  values [11]); (b) the same data plotted in logarithmic coordinate system [13].

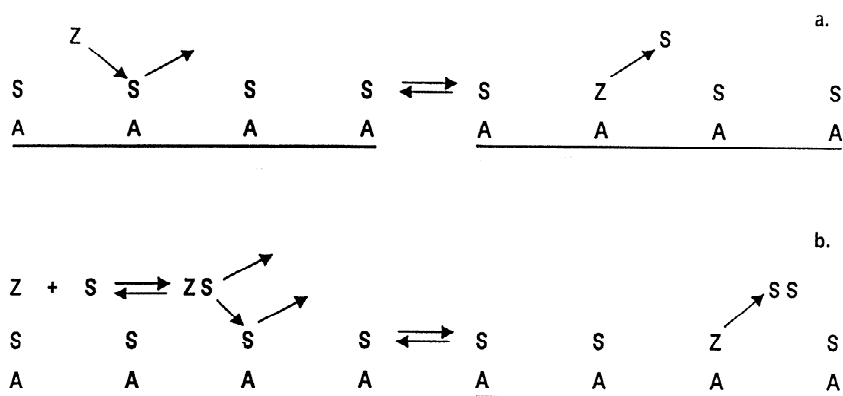
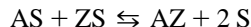


Fig. 6. Molecular mechanism of competitive adsorption (A — silanol group; S — modifier molecule; Z — solute molecule) (a) Simple displacement; (b) displacement combined with dissociation of solvate ZS.

solvated by the modifier, the adsorption of solute Z must then be accompanied by decomposition of the solvate ZS (Fig. 6b). The solvation of solute Z by the modifier S, i.e. formation of ZS complex, is competitive to adsorption of solute — formation of AZ complex. Adsorption of solute — formation of A–Z hydrogen bond — results in release of two molecules of modifier S:



$$K = \frac{X_{AZ} \cdot X_S^2}{X_{AS} \cdot X_{ZS}}$$

$$k = \frac{X_{AZ}}{X_{ZS}} = \frac{\text{const}}{X_S^2}$$

$$\log k = \text{const} - 2 \log [S] \quad (5)$$

so that (in case of strong solvation of solute by modifier) slope  $m=2$  in spite of single-point adsorption.

I sent my first paper from the “simple molecular adsorption model” series to Analytical Chemistry. Lloyd Snyder was one of the referees and after corrections of the manuscript according to his suggestions the paper appeared [13], bringing a record number of reprints requests. Although over 30 years have passed since its publication it is still regularly cited in the literature; the simple Eq. (4) is considered as very popular and convenient in method development [14,15]. It can also be derived from the simplified Snyder equation (Ref [12], Eqs .8–10a) for eluent strength of binary eluents [16]; in Snyder’s

model the slope  $m$  is equivalent to the ratio of molecular areas of solute,  $A_s$ , and modifier,  $n_b$ , however, since the molecular areas of H-bonding groups are anomalously large, the ratio  $A_s/n_b$  is usually low [17].

The investigation of retention vs. eluent composition relationships became one of the main directions of research in the Department of Inorganic and Analytical Chemistry of the Medical University of Lublin. Golkiewicz in his Ph.D. dissertation [18] investigated numerous solutes and modifiers for silica as adsorbent; analogous investigations for alumina were published by Wawrzynowicz [19] and for other polar adsorbents by Waksmundzka-Hajnos [20]. The investigations were very extensive; in the 1970s and 1980s the scientific equipment of the Department was very poor (most equipment was purchased by the Medical University for the clinics) and we were virtually limited to paper and thin-layer chromatography; the only chance to publish in international journals was to concentrate on physico-chemical theory of chromatography.

The abundant experimental data confirmed the competitive adsorption model of Snyder who in his later papers [21–24] considered the simple version as a special, extreme case of his theory relating to strong localisation of the solute molecule over an adsorption site and considered the two approaches as a common Snyder–Soczewinski model.

Eq. (4) was applied for practical method development and interpretation of molecular structural effects by numerous scientists; for instance, series of

papers have been published by Hara [25], Jandera [26], Palamareva [27], Petrovic [28] and others.

The simple adsorption model [13] was further developed in later papers [29,30]. It is based on simplifying assumptions (e.g., homogeneous adsorption centres, constancy of activity coefficients) and therefore inspired some physical chemists to derive more general relationships which take into account the real situation in the adsorbent and bulk phases [31–39]. The complex multiparameter equations simplify to Eq. (4) when simplifications are assumed.

#### 4. Reversed-phase systems

In reversed-phase systems of the type octadecyl silica/water+methanol the retention vs. eluent composition relationship of semilogarithmic type (Eq. (1a)) is usual, reported by Snyder et al. [40] in the form:

$$\log k = \log k_w - S \varphi_{\text{mod}} \quad (6)$$

However, for some solutes and eluents linear plots in the log–log co-ordinate system (Eq. (4)) have been reported. Thus, Murakami [41] found linear relationships for polar benzene derivatives (Fig. 7) and derived equation analogous to Eq. (4) in which

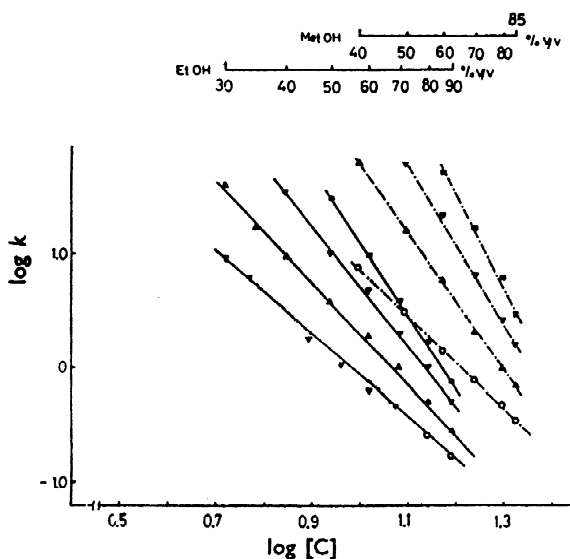


Fig. 7.  $\log k$  vs.  $\log C_{\text{mod}}$  of benzene derivatives for reversed-phase systems RP 18/water+methanol and RP 18/water+ethanol [41].

the slope  $m$  is related to the stoichiometry of sorption in the brush phase — the sum of modifier molecules displaced from the stationary film and lost by the solute molecule solvate upon adsorption — as in Fig. 6b. Geng and Regnier [42] applied this approach even to the sorption of large protein molecules (Fig. 8), Sadlej-Sosnowska and Sledzinska [43] found that

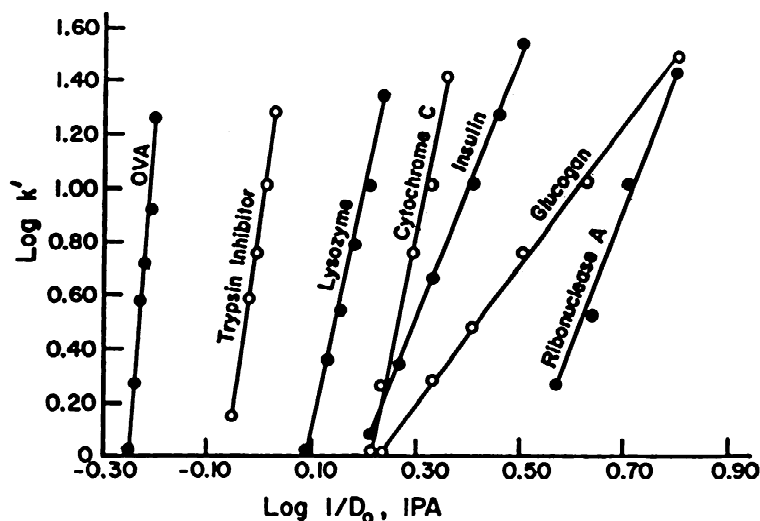


Fig. 8. Linear  $\log k$  vs.  $\log C_{\text{mod}}$  plots for the system RP 8–50% HCOOH in water+propanol-2 [42].

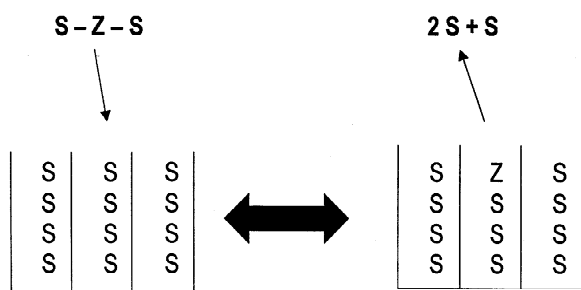


Fig. 9. Presumed mechanism of competitive sorption of solute combined with dissociation of  $ZS_2$  solvate (slope of  $\log k$  vs.  $\log C_{\text{mod}}$  plot  $m=3$ ). RP18 sorbent saturated with modifier (S) molecules.

for some steroids both Eq. (6) and Eq. (4) describe well retention vs. eluent composition relationships in aqueous RP systems with methanol and acetonitrile as modifiers which indicates that as in Ref [19], such investigations cannot verify either model.

The difficulty is due to the fact that  $k$  values can be determined by high-performance liquid chromatography (HPLC) only in a narrow range (say, 1–20) corresponding to narrow range of  $\varphi_{\text{mod}}$  values — especially in the case of high slopes  $m$ . Further examples of Eq. (4) in RP aqueous systems were reported by Shatts and Sakhartova [44]. It seems that in the RP systems some displacement mechanism may in some cases be operative, as in non-aqueous systems with polar adsorbents (Fig. 6b). The alkyl  $C_{18}$  chains bound to the surface are saturated with the modifier molecules, some of which are displaced by the adsorbed solute molecule which at the same time loses some of the solvating modifier molecules (Fig. 9). Fig. 9 represents a simplified picture of the molecular retention mechanism: vertical lines are  $C_{18}$  chains on ODS silica surface. The hydrophobic interaction of solute Z molecule (solvated with two modifier S molecules) with the hydrocarbon chains is accompanied by displacement of one modifier molecule from the surface film and loss of two solvating modifier molecules. The slope of the  $\log k$  vs.  $\log [S]$  line is then  $m=3$ .

## 5. Conclusions

The simple equations following from the applica-

tion of law of mass action to adsorption equilibria have been confirmed for non-aqueous eluents and polar adsorbents (silica, alumina, Florisil, bonded cyano-, amino- and diol adsorbents) in spite of gross simplifications assumed in their derivation. They permit interpolation and even extrapolation of experimental data obtained for few isocratic experiments for method development. The logarithmic relationship (Eq. (4)) has also been reported for aqueous reversed-phase systems.

The sophisticated physicochemical theories of adsorption result in multiparameter equations difficult for unambiguous verification and independent determination of their parameters, however, they may explain deviations from expected retention behaviour.

## References

- [1] R. Neher, in: B.G. Marini-Bettolo (Ed.), *Thin-Layer Chromatography*, Elsevier, Amsterdam, 1964.
- [2] D.L. Saunders, *Anal. Chem.* 46 (1974) 470.
- [3] V. Meyer, M.D. Palamareva, *J. Chromatogr.* 641 (1993) 391.
- [4] E. Soczewiński, C.A. Wachtmeister, *J. Chromatogr.* 7 (1962) 31.
- [5] W. Kemula, H. Buchowski, *Roczn. Chemii* 29 (1955) 178.
- [6] A.M. Rozen, in: A.P. Zefirov, M.M. Senyavin (Eds.), *Ekstraktsiya*, Vol. 1, Gosatomizdat, Moscow, 1962, p. 45.
- [7] E. Soczewiński, G. Matysik, in: *Intern. Symp. VI. Chromatogr. Electrophor. PAE*, Bruxelles, 1971, p. 203.
- [8] E. Soczewiński, G. Matysik, *J. Chromatogr.* 32 (1968) 458.
- [9] M. Ciszewska, E. Soczewiński, *J. Chromatogr.* 77 (1975) 21.
- [10] A. Waksmundzki, E. Soczewiński, Z. Suprynowicz, *Coll. Czechoslov. Chem. Commun.* 27 (1962) 2000.
- [11] A. Waksmundzki, J.K. Rózyło, *Chem. Anal. (Warsaw)* 11 (1966) 101.
- [12] L.R. Snyder, *Principles of Adsorption Chromatography*, Marcel Dekker, New York, 1968.
- [13] E. Soczewiński, *Anal. Chem.* 41 (1969) 179.
- [14] A. Rizzi, Retention and selectivity, in: E. Katz, R. Eksteen, P. Schoenmakers, N. Miller (Eds.), *Handbook of HPLC*, Marcel Dekker, New York, 1998, p. 1.
- [15] M. Caude, A. Jardy, *Normal Phase Chromatography*, *ibid.*, pp. 325–363.
- [16] E. Soczewiński, W. Golkiewicz, H. Szumilo, *J. Chromatogr.* 45 (1969) 1.
- [17] E. Soczewiński, T.H. Dzido, *Chromatographia* 22 (1986) 25.
- [18] E. Soczewiński, W. Golkiewicz, T. Dzido, *Chromatographia* 10 (1977) 221.
- [19] T. Wawrzynowicz, T.H. Dzido, *Chromatographia* 11 (1978) 335.

- [20] M. Waksmundzka-Hajnos, *Chem. Anal. (Warsaw)* 43 (1998) 301.
- [21] L.R. Snyder, *Anal. Chem.* 46 (1974) 1384.
- [22] L.R. Snyder, H. Poppe, *J. Chromatogr.* 184 (1980) 363.
- [23] L.R. Snyder, in: C. Horvath (Ed.), *High-Performance Liquid Chromatography — Advances and Perspectives*, Academic Press, New York, 1983, p. 157.
- [24] L.R. Snyder, J.W. Dolan, *Adv. Chromatogr.* 38 (1998) 115.
- [25] S. Hara, Y. Fujii, M. Hirasava, S. Miyamoto, *J. Chromatogr.* 149 (1978) 143.
- [26] P. Jandera, M. Kucerova, J. Halikova, *J. Chromatogr. A* 762 (1997) 15.
- [27] M. Palamareva, I. Kozekov, *J. Planar Chromatogr.* 9 (1996) 439.
- [28] S.M. Petrovic, E. Loncar, M. Popsavin, V. Popsavin, *J. Planar Chromatogr.* 10 (1997) 406.
- [29] E. Soczewinski, *J. Chromatogr.* 130 (1977) 23.
- [30] E. Soczewinski, *J. Chromatogr.* 388 (1987) 91.
- [31] M. Verzele, F. Van Damme, C. Devaele, M. Ghijs, *Chromatographia* 24 (1987) 302.
- [32] J.E. Paanakker, J.C. Kraak, H. Poppe, *J. Chromatogr.* 149 (1978) 111.
- [33] E.H. Slaats, J.C. Kraak, W.J.T. Brugman, H. Poppe, *J. Chromatogr.* 149 (1978) 255.
- [34] M. Jaroniec, D.E. Martire, M. Borówko, *Adv. Colloid Interface Sci.* 22 (1985) 177.
- [35] M. Jaroniec, D.E. Martire, *J. Chromatogr. A* 655 (1993) 37.
- [36] W. Rudzinski, *Retention in liquid chromatography*, in: J.A. Jónsson (Ed.), *Chromatographic Theory and Basic Principles*, Marcel Dekker, New York, 1987, Chapter 6.
- [37] W. Rudzinski, J. Michalek, J.A. Jónsson, *Chromatographia* 22 (1986) 337.
- [38] D.E. Martire, R.E. Boehm, *J. Liq. Chromatogr.* 3 (1980) 753.
- [39] P. Jandera, J. Churacek, *J. Chromatogr.* 91 (1974) 277.
- [40] L.R. Snyder, J.W. Dolan, J.R. Gant, *J. Chromatogr.* 165 (1979) 3.
- [41] F. Murakami, *J. Chromatogr.* 178 (1979) 393.
- [42] X. Geng, F.E. Regnier, *J. Chromatogr.* 296 (1984) 15.
- [43] N. Sadlej-Sosnowska, I. Sledzinska, *J. Chromatogr.* 595 (1992) 53.
- [44] V.D. Shatts, O.V. Sakhartova, *High Performance Liquid Chromatography*, Zinatne, Riga, 1988, (in Russian).