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Control of dispersion in capillary electrochromatography coupled to UV and mass spectrometric detection

Robert J. Boughtflower[a,*], Clare J. Paterson[a], John H. Knox[b]

[a]*Separation Science Group, Physical Sciences, GlaxoWellcome, Gunnels Wood Road, Stevenage, SG1 2NY, UK*

[b]*Department of Chemistry, University of Edinburgh, Edinburgh, UK*

Abstract

Capillary electrochromatography (CEC), along with other miniaturised chromatography techniques, such as capillary LC, offers the most benefit when efficiently coupled to mass spectrometric (MS) detectors. In conventional one-piece CEC columns, dispersion in the open connecting tube between the packed column and MS source reduces chromatographic performance to unacceptable levels. This paper examines the effect on dispersion of various column-tube arrangements and offers suggestions as to the most practical way of connecting CEC–UV–MS. Comparisons of theoretical and measured values for these different arrangements are shown.

Keywords: Dispersion; Detection, CEC; Band spreading

1. Introduction

CEC is a rapidly developing separation technique that offers enormous promise for the future of miniaturised chromatography. Since the demonstration of CEC [1,2] and more detailed work on the theoretical background [3–5], several groups have demonstrated its usefulness in various applications [6–16]. Its use, as is common for relatively new techniques, is increasing rapidly. However, there are currently operational restrictions, such as poor on-column UV sensitivity and column fragility, which can make CEC a challenging technique and ultimately limit its usefulness. Most of the problems surrounding CEC arise from the use of a one-piece column composed of a single length of fused-silica capillary. Injection and detection of the sample is carried out within the column, thus the ''cell'' path length is effectively limited to the diameter of the capillary. This capillary is packed with a stationary phase, which is retained within the capillary via the fabrication of two frits, usually by thermal treatment of the stationary phase in a hot filament device [17]. Unfortunately, fabrication of these frits and more importantly a UV detection window, removes the polyimide coating on the fused-silica and makes this section of the column fragile. Ideally it would be desirable to detect out of the column itself via connection of the separation part of the column to an independent detector (cell) [16,18]. However, it has been demonstrated previously that solute bands travelling from the packed to the open (detection) part of the capillary suffer significant loss of efficiency in a one-piece column [19]. It has been proposed [20] this is due to discontinuities in field strength and flow velocity resulting from the change in flow profile at the interface between the packed and open parts of the tube. Nevertheless, it is still a

*Corresponding author.

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highly desirable requirement that CEC separation, preferably with some form of on-line optical detection (normally UV), can be connected to mass spectrometers (MS) without too much loss in chromatographic performance. The goal of this work is to investigate the possibilities of making CEC column connections to open tubes and yet enable performance losses to be minimised, so that the use of CEC–UV–MS can become a workable reality.

2. Band spreading in the open tube following CEC

As mentioned above, it seems apparent that open tube sections of the same diameter as the packed part of the tube cause unacceptable dispersion in CEC. In a typical configuration the column is a one piece arrangement with the electric field across the whole column, i.e., from the inlet of the packed column to the outlet of the open tube section. The exact nature of the flow profile as a solute band exits from the packed to the open section is not well understood, but Rathore and Horváth [20] have recently proposed models which strongly support recent imaging of these processes. Other factors that affect the operational arrangement of the CEC system are also important. To realistically couple rapid CEC separations to sensitive MS based detection systems, it would be preferable not to dilute the field strength across the whole column, but simply to apply the field across the packed section of the column. It is certainly possible to ground the column at the connection interface to the open tube, but this would mean that the flow profile would revert to that attained from entirely pressure flow in the open tube. Dispersion would then be appreciably worse under these circumstances. To ascertain the effect on efficiency of adding a length of open tube of varying diameter to the CEC column we need to add the volume variances of each component of the system, and thus calculate the total variance of the system. Tables 1 and 2 show the symbols and typical values used throughout the calculations.

Plate height for the open tube is calculated from the Taylor equation (or Golay equation with $k'=0$)

Table 1
Symbols and typical values for CEC parameters used throughout the calculations

CEC parameters	Symbol/eq.	Typical value
Packed tube diameter	D	100 μ
Packed tube length	L	200 mm
Bed porosity	ϵ	0.6
Elution time (unretained solute)	t_m	200 s
Linear flow-rate	$u=\frac{L}{t_m}=\frac{4F_v}{\pi D^2}$	1 mm/s
Number of plates	$N=\frac{L}{H}$	100 000
Plate height	H	2 μ[a]
Volume flow-rate	$F_v=\frac{\pi D^2 \epsilon u}{4}=\frac{\pi D^2 \epsilon L}{4t_m}$	0.4 μl/min[a]
Length standard deviation	$\sigma_{z,col}=(HL)^{1/2}=\frac{L}{N^{1/2}}$	0.6 mm[a]
Volume standard deviation	$\sigma_{v,col}=\left(\frac{\pi D^2 \epsilon}{4}\right)\frac{L}{N^{1/2}}$	3 nl[a]
Volume variance from column	$\sigma^2_{v,col}=\left(\frac{\pi D^2 \epsilon}{4}\right)^2\frac{L^2}{N}$	

[a] Calculated.

Table 2
Symbols and typical values for open tube parameters used throughout the calculations

Open tube parameters	Symbol/eq.	Typical value
Open tube diameter	d	25 μ
Open tube length	L_t	100 mm
Diffusion coefficient	D_m	10^{-9} m^2/s
Peak width (at half height)	$P_{w1/2}$	2 s[a]
Linear velocity	$u_t = \frac{4F_v}{\pi d^2}$	14 mm/s[b]
Volume standard deviation	$\sigma_{v,tube} = (H_t L_t)^{1/2}\left(\frac{\pi d^2}{4}\right)$	10 nl[b]

[a] Measured.
[b] Calculated.

$$H_t = \frac{d^2 u_t}{(96 D_m)} = \frac{F_v}{24\pi D_m} = \frac{D^2 \epsilon u}{(96 D_m)} = \frac{(\sigma_{z,tube})^2}{L_t} \quad (1)$$

Length standard deviation:

$$\sigma_{z,tube} = (H_t L_t)^{1/2} = \frac{P_{w1/2} u_t}{2.355} \quad \text{(calculated from data)} \quad (2)$$

Volume standard deviation:

$$\sigma_{v,tube} = (H_t L_t)^{1/2}\left(\frac{\pi d^2}{4}\right) \text{ (calculated from data)} \quad (3)$$

Volume variance from column:

$$\sigma^2_{v,col} = \left(\frac{\pi D^2 \epsilon}{4}\right)^2 \frac{L^2}{N} \quad (4)$$

Volume variance from tube:

$$\sigma^2_{v,tube} = H_t L_t \left(\frac{\pi d^2}{4}\right)^2 = \frac{\pi^2 D^2 \epsilon u L_t d^4}{(96)(16 D_m)} = \frac{\pi^2 D^2 \epsilon L L_t d^4}{(96)(16 D_m t_m)} \quad (5)$$

The combined variance from the combined column and tube [Eqs. (4) and (5)] is then given by:

$$\sigma^2_{v,tot} = \sigma^2_{v,col} + \sigma^2_{v,tube} = \sigma^2_{v,col}\left(1 + \frac{\sigma^2_{v,tube}}{\sigma^2_{v,col}}\right) = \sigma^2_{v,col}\left(1 + \left(\frac{L_t}{L}\right)\left(\frac{d}{D}\right)^2\left(\frac{d^2}{D_m t_m}\right)\left(\frac{N}{96\epsilon}\right)\right) \quad (6)$$

If we substitute in some typical values into Eq. (6), and for this calculation choose a smaller column diameter such as 25 μ then we have:

$$\frac{L_t}{L} = \frac{1}{2}; \quad \frac{d}{D} = \frac{1}{4}; \quad d = 25 \times 10^{-6} \text{ m};$$

$$D_m = 10^{-9} \text{ m}^2/\text{s}; \quad t_m = 200 \text{ s}; \quad N = 10^5; \quad \epsilon = 0.6$$

Then for these values:

$$\sigma^2_{v,total} = (1 + 0.17) \times \sigma^2_{v,col} = 1.17\sigma^2_{v,col}$$

That is, the ‘‘extra column’’ dispersion adds 17% to column dispersion itself, so efficiency is reduced by 17% and resolution (proportional to $\sqrt{N}$) by about 8%. In what follows we call the factor 1.17 the ‘‘dispersion factor’’. The effect of choosing different diameters of the open tube when $L_t/L = 1/2$, with a main CEC column of 100 μm diameter is shown in Table 3. To get less than 20% additional dispersion, the tube diameter must be less than about 25 μm. Eq. (6) shows that the dispersive effect of additional tubing is extremely sensitive to its diameter (factor

Table 3
Calculated dispersion factor when open tubes of different diameter are connected to 100 μm bore CEC columns for $L_t/L = 1/2$

Diameter (μm)	50	40	30	25	20	15	12	10
Dispersion factor (column dispersion is 1)	3.71	2.11	1.35	1.17	1.069	1.022	1.009	1.004

d^4) but relatively insensitive to its length (factor $(L_t/L)^1$, so it is the tube diameter which must be carefully considered in making any connection of CEC to a distant piece of equipment. These calculations, of course, make no allowance for any dispersion which will arise from joins between tubes whether of the same or of different diameters.

3. Experimental

3.1. Instrumentation

A Hewlett-Packard (Waldbronn, Germnay) HP^{3D} CE (with CEC vial pressurisation) was used throughout. All one-piece CEC columns used were 100 μm internal diameter (I.D.) and approximately 375 μm outer diameter (O.D.) containing Waters Spherisorb C6/SCX mixed-mode stationary phase (Innovatech, Stevenage, UK). Unless otherwise stated the columns were 30 cm in length. Due to the nature of this work, which involved multiple runs on each column system, occasional breakage of the inlet frit was inevitable. If this occurred a new frit was fabricated [17] as close as possible to the original. Any adjustments to field strength were made accordingly. No particular attempt to correct the data for packed length was made, as any resulting effects were insignificant. When column connections were used, they were fabricated where possible from the original one-piece column, which was cut at the retaining frit and this end was polished using a simple home-made polishing unit. This column was connected to the open tube section, which was also polished at the connection end. The connections were made by a small piece of PTFE tubing of slightly smaller I.D. than the capillary O.D. This facilitated a ''tight'' fit but care was taken to ensure no swarf from inside the PTFE tubing blocked the connection of the capillary ends. In cases where the electrical connection was made at the connection point, the open tube part of the capillary was painted with a graphite paste (''Leit C'', Protana, Denmark). This covered the end face of the capillary and a suitable length of the outside tube, to a point where a convenient electrical earth could be connected via a brass connector as shown in Fig. 1. Open tube lengths varied according to the necessary distance required between the column end frit and the detection position. The overall length of the whole column for these experiments was equal to the packed column length + extra open tube length to detection point + 8.5 cm (open tube from detector to cathode).

All runs were performed with the mobile phase vials pressurised to 12 bar and columns were initially conditioned at an applied voltage of 15kV under these conditions. The mobile phase vials were replaced regularly to avoid buffer depletion. All samples were injected electroendosmotically. Due to the variable overall column length, the injection conditions were 260 v/cm for 10 s (for a 30 cm one-piece packed column this was typically 10 kV for 10 s).

The mass spectrometer used was a Hewlett-Packard 1100 series MSD fitted with the CE electrospray interface.

3.2. Chemicals and materials

The mobile phase employed throughout these experiments was acetonitrile (ACN)–50 m*M* NaH_2PO_4 (pH 3.5), 50:50. The buffer pH was adjusted with phosphoric acid, prior to mixing with the ACN. Both monobasic sodium phosphate and phosphoric acid were obtained from BDH (Poole, UK). The ACN was obtained from Rathburn Chemicals (Walkerburn, Scotland, UK). The chromatography test mixture used for the separations and subsequent data measurement was composed of (1) thiourea (flow marker), (2) benzamide, (3) anisole, (4) benzophenone and (5) biphenyl (in order of elution) all dissolved at 0.5 mg/ml in the mobile

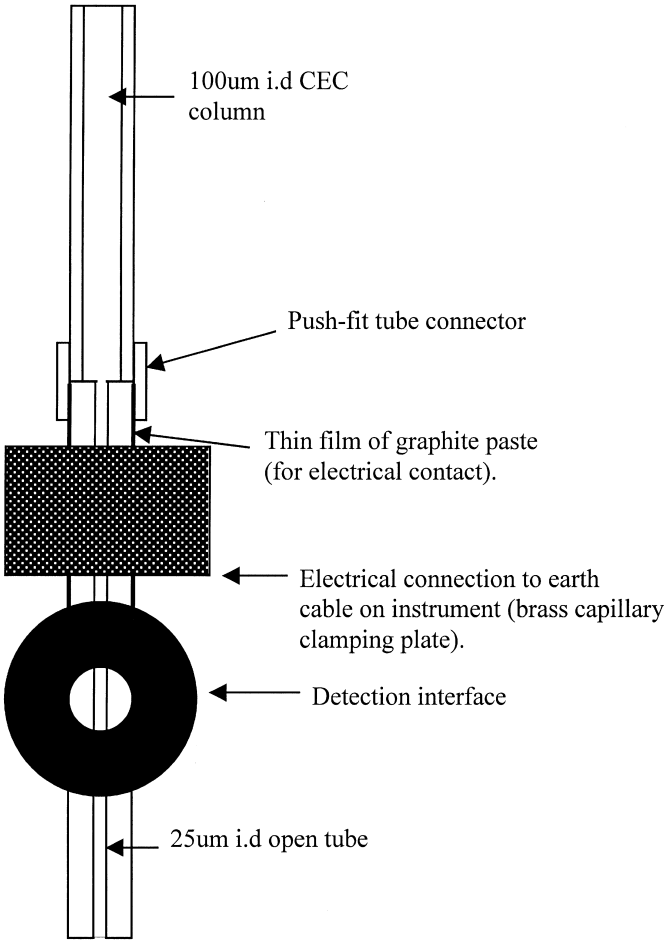

Fig. 1. Schematic diagram of column to capillary joining utilising electrical earth connection at join.

phase. All of these compounds were obtained from Aldrich (Gillingham, UK). The pharmaceutical mixture used for the CEC–UV–MS separation was composed of thiourea, phenytoin, prednisolone, methyl-prednisolone, caffeine, testosterone, amoxillicin and cefatrizine at a concentration of 125 μg/ml for each compound, also in order of elution. All compounds were obtained from Sigma–Aldrich UK.

3.3. Experimental design

The primary objective of the experimental work was to measure the additional dispersion factor resulting from various configurations of the open tube leading to the detection system, which necessarily follows the frit terminating the CEC column. The different configurations which have been examined are shown in Fig. 2. Experiment 1 (Fig. 2a) investigated the dispersion with a simple extension of the packed column by open tubing of the same bore. Three positions of the detector window were examined ranging from very close to the frit (normal position denoted by *N*), 10 and 25 cm from the frit (denoted by *R* and *S*).

For experiment 2, the first detection measurement was carried out using the one-piece column from experiment 1. Detection was performed at 3 cm from

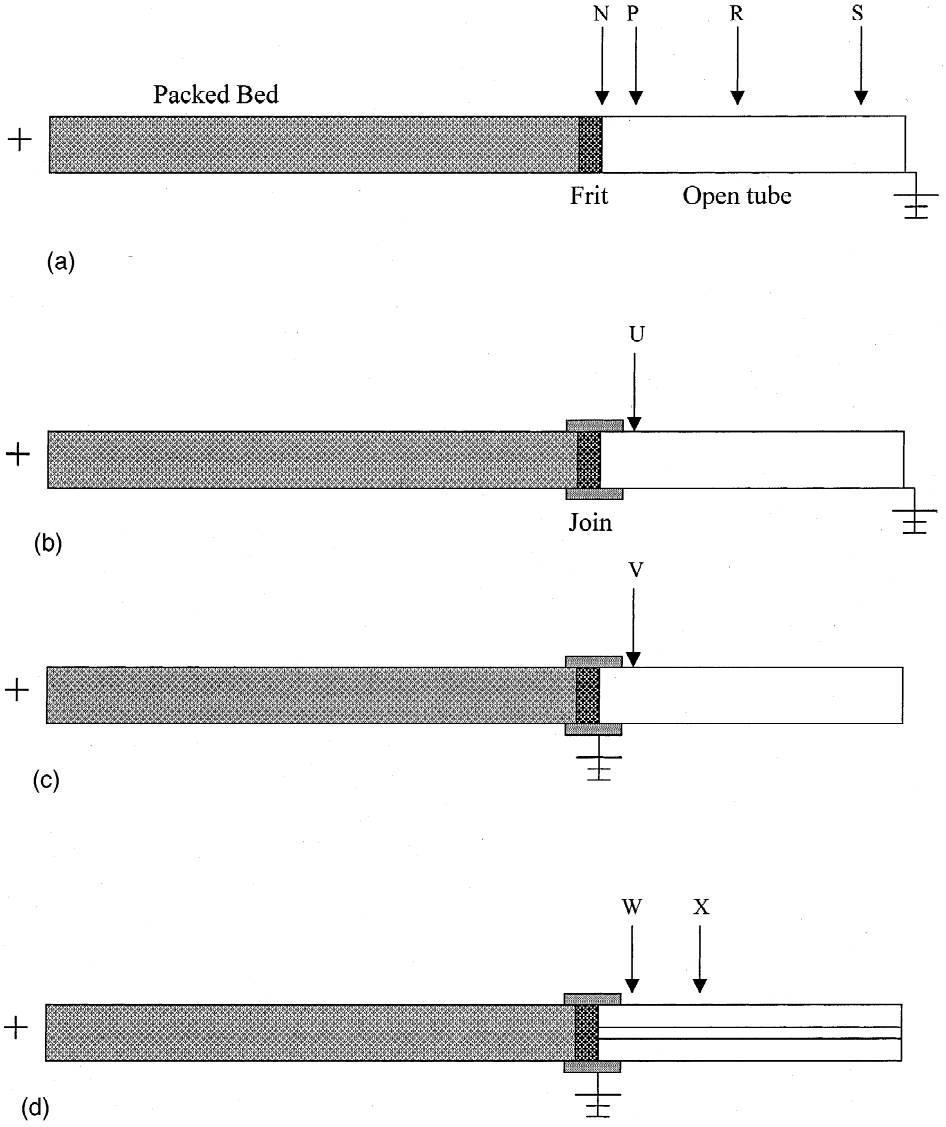

Fig. 2. Various columns/tube layouts for different dispersions (a,b,c,d).

the retaining frit at a point *P* illustrated in Fig. 2a. These measurements were used as ''unbroken column'' reference values to compare the effects of column joining carried out in experiment 2.

In experiment 2 (Fig. 2b) the CEC column was coupled to an open tube of the same diameter by means of a join and sleeve. The earth connection could then be made either at the join (Fig. 2c) or at the end of the open tube (Fig. 2b). Detection measurements were performed at distances of 3 cm from the frit at points labelled *V* and *U*, respectively.

In experiment 3 (Fig. 2d) the bore of the open tube was reduced to 25 μm. Detection was at 3 and 10 cm from the frit.

Dispersion values for detection at *N* in experiment 1, were used in all subsequent experiments as reference values for the peak variance produced by the packed column alone. For experiments 2 and 3

this original column was cut at the frit and joined to the 100 and 25 μm open tubes.

3.4. Observations of joining columns

When the earth connection is made at the join of the column and the open tube, the electroosmotic flow before the join is replaced by hydraulic flow after the join, the volume flow-rate remaining the same. The hydraulic flow then causes a pressure drop across the open part of the tube. This is readily calculated from the Poiseuille equation:

$$\Delta p = 32\eta L u_{\text{tube}} / d_c^2$$

for typical values, $\Delta p \cong 1 \times 10^5$ N/m^2 or about 1 atmosphere. This means that fairly simple push-fit tubing type connections may be used even if we decide in practice to use significantly longer lengths of connecting tube.

Additionally, when a CEC column is connected ''on-line'' via a push-fit connection, into a connecting tube with the electrical earth made at this join, we have an ''on-flow'' electrode system. This means that any gaseous products of electrolysis will travel down the tube. Hydrogen gas may be produced at the cathode connection and interfere with any downstream optical detection. This means careful consideration needs to be given to the precise layout of the earth connection with respect to any optical detection. The stability of the experiments carried out in this manuscript suggest that the slight Δp generated by the small diameter connection tubing would be enough to prevent this being a significant problem. It is interesting to consider whether this bubble generation could be used advantageously to measure volumetric flow-rates with acceptable accuracy in these systems.

4. Results and discussion

4.1. Dispersion factors for different CEC column/open tube configurations

The following results are given as ''dispersion factors'' representing the ratio of (the total volume variance) to (the volume variance measured at *N*). The total variance therefore includes any extra dispersion measured at the detection point. The total variance will also reflect any dispersion arising from physical connections. The capital letters in the title bar of the result tables refer to the relevant detection points in each experiment as shown in Fig. 2.

4.2. Experiment 1

This experiment was performed to measure the amount of dispersion in normal CEC operation in a one-piece column. Test mixture separations were carried out and detection at different distances from the frit were compared. This work was performed at a field strength of 450 V/cm.

It can be seen from Table 4 that there is extensive dispersion associated with the solute bands travelling through the open tube section of the column. Also, that this dispersion appears to increase quite soon after the frit. This would be too much loss in performance to tolerate, as the distances shown are likely to be smaller than the ''real'' distances needed to connect to a mass spectrometer.

4.3. Experiment 2

This experiment was performed to assess the contribution to dispersion made by the connections of the packed column to the open tube, and also the effect of making the earth connection at this point, instead of at the end of the open tube section. The data in Table 4 suggests the profile of the solute band appears to degrade rapidly as it emerges from the packed section into the open tube, for a conventional one-piece column arrangement. Therefore, in experi-

Table 4
Dispersion factors for a 100 μm one-piece column with detection at different distances from the frit (Experiment 1)

Peak	Volume variances (nl^2)					Dispersion factor	
	N	*R*	*R–N*	*S*	*S–N*	*R*	*S*
1	36	136	100	247	211	3.77	6.86
2	42	150	108	287	245	3.54	6.77
3	72	158	86	265	197	2.20	3.67
4	92	199	107	360	268	2.17	3.94
5	150	243	93	363	213	1.62	2.42
Mean	–	–	99	–	226	–	–

ment 2 detection was attempted as close to the frit as practically possible, limited only by the physical distance between the frit and the connection tubing and detection interface (minimum 3 cm, see Fig. 2). When the earth is made at the connection point (as it is for data shown in column *V*), there is no electrical field across the open tube section of the capillary and therefore there will be only pressure-derived flow in the open section. This should degrade the performance further still. The data in this experiment was obtained by operating a similar column at a different field strength of 740 V/cm using column arrangements described in Fig. 2b and c, results are shown in Table 5.

As expected, the results from experiment 2 show that the dispersion increases as physical connections are made between capillaries and also if the electrical earth is made at the connection point. There is a tendency for the later eluting peaks to show higher variance values than expected, this is particularly evident when the electrical earth is made at the join and hydraulic flow exists in the open tube. These experiments are for packed and open tube sections of the same diameter. As predicted from experiment 1 the dispersion in these systems was too great and would only be significantly worse under these experimental conditions. However, it is interesting to note that connections between capillaries can be made, where the contribution from the actual join appears to be of the same order as the losses incurred in the first 3 cm of the open tube. Much more significant losses are seen when the electrical connection is made at the join.

4.4. Experiment 3

This experiment was again performed at 740 V/cm field strength using a 100 μm diameter packed column but connected to a 25 μm diameter open tube. The same measurements of dispersion, as in previous experiments, were made at detection distances of 3 and 10 cm from the retaining frit. Results are shown in Table 6.

Table 6
Dispersion factors for a 100 μm column joined to 25 μm open tube with electrical earth at the join (Experiment 3)

Peak	Volume variance (nl^2)				Dispersion factor	
	N	*W*	*X*	*X–W*	*W*	*X*
1	44	62	76	14	1.41	1.74
2	52	56	63	7	1.07	1.21
3	70	57	78	21	0.80	1.11
4	86	64	101	37	0.75	1.18
5	121	89	150	61	0.73	1.24
Mean	–	–	–	37	–	–

The results obtained from Experiment 3 suggest that the dispersion observed within the 25 μm open tube is reduced considerably compared to the tube of equal diameter to the packed column. The values for extra variance obtained between the 3 and 10 cm detection points in the 25 μm open tube are very variable, especially for later retained peaks, and the reason for this is not clearly understood. From calculated values for the 25 μm tube we should expect about 12 (nl^2). The values of dispersion factors less than unity shown in column *W* are probably a result of there being less dispersion associated with detection in 25 μm, at only 3 cm away from the join, than inherently occurs in normal detection at a ''finite'' distance from the frit. It is clear from both experiments 1 and 2 that the solute band profile in conventional CEC is deteriorating rapidly, so it seems highly plausible that even

Table 5
Dispersion factors for a 100 μm column (Fig. 1b) with detection at 3 cm and different electrical earth points (Experiment 2)

Peak	Volume variances (nl^2)							Dispersion factor		
	N	*P*	*P–N*	*U*	*U–N*	*V*	*V–N*	*P*	*U*	*V*
1	44	71	27	98	54	144	100	1.62	2.25	3.30
2	52	82	30	107	55	148	96	1.57	2.05	2.83
3	70	89	19	119	49	184	114	1.26	1.69	2.61
4	86	116	30	152	66	238	152	1.36	1.77	2.78
5	121	161	40	191	70	285	164	1.32	1.57	2.35
Mean	–	–	29	–	59	–	125	–	–	–

''normal'' detection includes significant inherent dispersion.

If the measured values of tube induced variance, represented as average peak volume variances (for all peaks except the flow marker) are compared to the values expected from the Taylor equation for laminar flow:

$$\sigma^2_{v,\text{tube}} = L_t \pi d^4 \frac{F_v}{384 D_m}$$

the following results are obtained (see Fig. 3).

For detection distances between *N* (0) and 3, 10 and 25 cm away from the packed column end frit, variance values of 76, 254 and 636 (nl^2) are expected from the Taylor equation with laminar flow. Measured values (from experimental set up Fig. 2a) are 30, 100 and 230 (nl^2), calculated as averages from the values given in Table 4. This suggests that the flow profile in the open tube when the field is across the whole column (Fig. 2a), is somewhere in between ''EOF derived plug-flow'' and laminar flow. For comparison purposes, data was also obtained for the same 3 cm detection distance but with the electrical earth made at the column join. This produces pure laminar flow in the connecting tube. Here the peak volume variance was measured as 86 (nl^2), calculated from average values given in Table 5, corrected for the effects of the join. This compares well with the calculated value of 76. This data and the earlier data shown of dispersion factors, support the model of laminar dispersion according to Taylor.

4.5. Dispersion associated with CEC–MS coupling

The data shown previously supports the principles of using smaller diameter connecting tubes when coupling CEC columns to remote detectors. However, to make on-line comparisons of UV and MS peak widths, it was impractical to use the UV data obtained through the 25 μm tube due to lack of detection sensitivity. For the purpose of this experiment detection was carried out in the 100 μm open

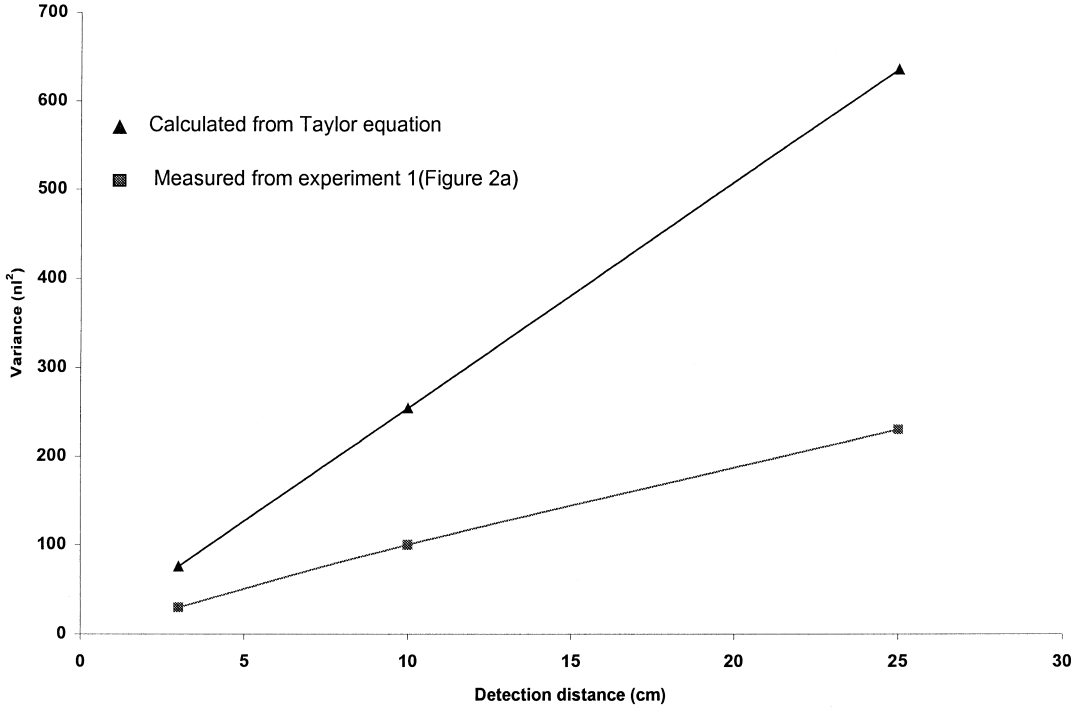

Fig. 3. Graph to compare extra peak volume variance obtained when detecting at variable distances from end frit in a conventional CEC system (i.e., electrical field across the whole column), with that predicted from the Taylor equation (for only laminar flow) for a 100 μm one-piece column.

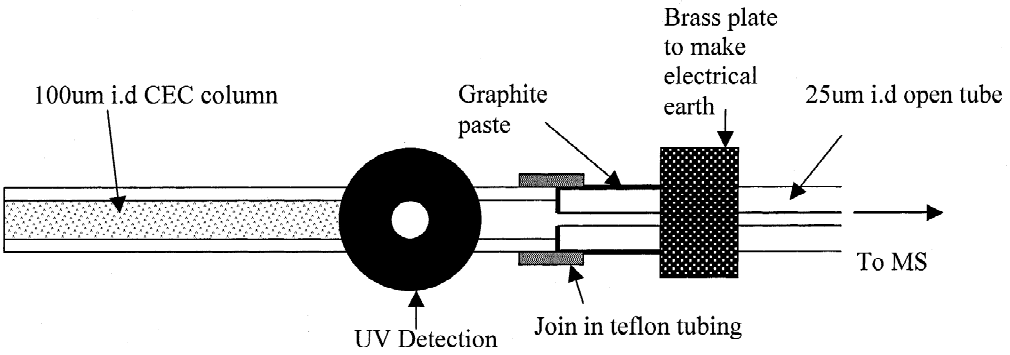

Fig. 4. Schematic arrangement of column, detector and connecting tube arrangements for comparing peak variances between UV and MS detectors.

tube just after the frit in a standard CEC column. This column was then joined to a length of 25 μm tube of approximately 75 cm, as shown in Fig. 4. This allowed measurements of the peak widths by UV and MS detection, to be carried out on-line from the same chromatographic run of three test components (caffeine, prednisolone and dexamethasone, in order of elution), shown in Fig. 5. The dispersion data is shown in Table 7.

The dispersion factor shown is calculated from the ratio of the volume variances at the MS and UV detectors. From a theoretical standpoint the expected minimal dispersion factor for the coupled system shown would be 1.255. This would be based on the assumption that a ''perfect join'' existed between the CEC column and the 25 μm diameter joining tube, and that only Taylor dispersion in the joining tube contributed to extra band broadening. This type of join is not possible in this experimental set up. In the case here, extra dispersion is introduced by the short length of 100 μm tube between the connection and detection points (detection volume) and by the joint connection itself. It is possible to make reasonable corrections for this extra dispersion. These corrections, have either been measured in experiments earlier in this manuscript or calculated. Volume variances of at least 30, 30 and 50 (nl^2) are introduced by the detection volume, capillary join and Taylor dispersion through the connecting tube, respectively. The first peak is also unexpectedly broad at the MS, which is probably due to sample overload. When corrections for these extra column effects are made we have dispersion factors for peaks 2 and 3 of 1.37 and 1.35, respectively. These values are in good agreement with those expected from the theoretical predictions, considering the difficulty in fabricating a consistent electrically earthed join between the capillaries.

This data supports the use of the column with smaller diameter connection tubing (at least a quarter of the diameter of the separation column) and the minimum length that is practical, to connect to a mass spectrometer. Ideally, for on-line UV detection to be performed, it should be carried out immediately after the retaining frit. Due to the lack of sensitivity in detecting optically through such small diameter capillaries, it is desirable to utilise a higher sensitivity cell as has been reported previously [16,18].

5. Conclusions

This paper demonstrates that using conventional CEC arrangements of one-piece columns with UV post-frit detection, it is imperative to detect as close as is practically possible to the frit itself. Even adopting this strategy, there is likely to be significant dispersion introduced. When coupled column and tube systems are used with the electrical field earthed at the joining point, dispersion in the tube can be predicted, to within a reasonable degree of experimental error, by using the Taylor equation. If connection, via a coupled tube, to a mass spectrometer is desirable it is strongly advised that the diameter of the connecting tubing is at least a quarter of the separation column diameter, smaller if practically

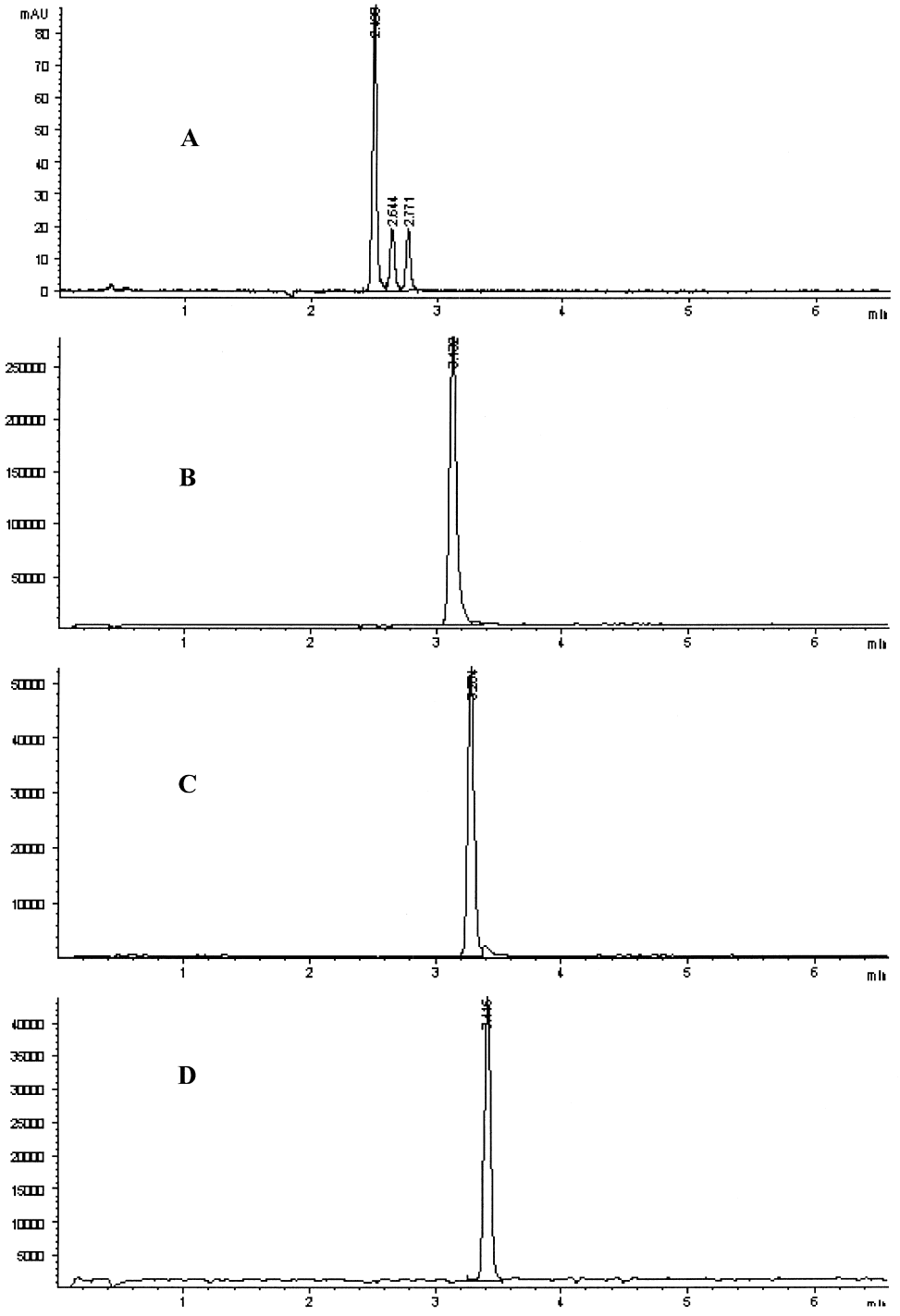

Fig. 5. Chromatograms obtained from coupled CEC–UV–MS system. Chromatogram A is on-line UV signal (215 nm). B, C and D are the SIM MS signals for caffeine (MH^+ 195), prednisolone (MH^+ 361) and dexamethasone (MH^+ 393), respectively. Mobile phase, MeCN–20 m*M* NH_4OAC (pH 4), 60:40; applied field, 25 kV; injection, 10 kV for 5 s.

Table 7
Comparison of peak volume variances obtained at the UV and MS detectors for 100 μm CEC column coupled to the MS with 75 cm of 25 μm tube

Peak	Volume variance (nl^2)		Dispersion factor
	UV	MS	
1	114	366	3.21
2	135	283	2.10
3	137	298	2.17

possible. It is possible to combine both these strategies to couple the CEC separation to UV detection in a higher sensitivity cell and subsequent detection in the mass spectrometer. Current UV cell designs would benefit from changes to enable more effective connections for flat-ended capillaries and the possibility to make the electrical earth at the outlet connection. These minor modifications should allow CEC–UV–MS to become a routinely used technique.

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