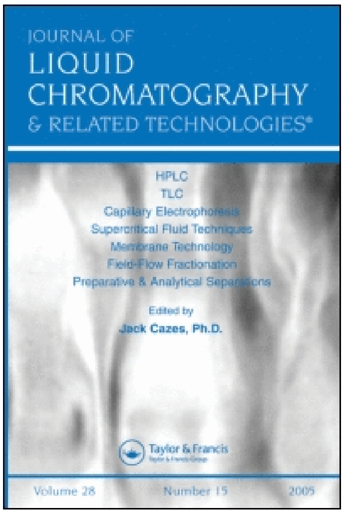

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EVALUATION OF A THERMAL PULSE FLOWMETER FOR QUANTITATIVE SIZE EXCLUSION CHROMATOGRAPHY

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ABSTRACT

The objective of this paper is to show an evaluation of the accuracy and precision of mobile phase flow rate measurement for size exclusion chromatography (SEC) using a thermal pulse flowmeter (TPF). The TPF measures flow by generating a pulse of heat in the liquid and determining the time required for it to be transported downstream to a fixed thermistor. The paper emphasizes development of a generally applicable method of assessing the TPF. The first method examined involved attaching a high precision syringe pump to the TPF to control input. Different responses were obtained with different solvents. Also, pulse transport time reproducibility as a function of solvent flow rate was determined and explained using error propagation analysis. However, with the very low values of error variance involved, uncertainties originated from the performance of the syringe pump system and SEC requirements. Therefore, the second method of evaluation selected was to correct actual SEC data using the TPF and to compare molecular weight averages to the known values. One calculation option was chosen and showed that, for this, particular rather noisy high temperature SEC system, the flow rate correction significantly improved accuracy of M_n but slightly worsened accuracy of M_w as well as precision of the averages. This second evaluation method, use of SEC data, is recommended over off-line approaches.

INTRODUCTION

Flow rate monitoring of the mobile phase has become progressively more important in size exclusion chromatography (SEC). For many years high resolution columns have required high reproducibility in flow rates. More recently, molecular weight and intrinsic viscosity detector systems have required that, in addition, the actual flow rate be known (i.e. high accuracy) so that concentration (g of polymer per cc) and not merely weight fraction per retention time increment can be calculated at each point on the chromatogram. The thermal pulse flowmeter (TPF) is currently the primary candidate instrument for accomplishing the needed measurement (1-11). This instrument measures flow rate by measuring the time required for a pulse of heat into the fluid to be carried a fixed distance. This "pulse transport time" is calibrated with flow rate measured by some other, independent method, in order to provide a TPF calibration curve.

The objective of this paper is to show an evaluation of the accuracy and precision of mobile phase flow rate measurement in SEC using the TPF. It is not meant to be the "final word" on the performance of the instrument. Our chromatographic system was unusually noisy during the study, probably because of column degradation. Also, with the rapid rate of technology development, it is likely that the particular TPF instrument used in this study will be superseded by the time this paper is published. Furthermore, this commercial version of the instrument was different in some technical details from previous research versions. Rather, the underlying reason for publishing the work is to show the method of evaluation. This method, perhaps with some modifications, should provide one systematic basis for evaluating future versions of the TPF and competitive instrumentation.

The work is presented in three main parts: an assessment of the need for flow rate measurement; determination of the accuracy and precision of the flowmeter via a specialized bench scale experiment and assessment of the SEC results obtained by flow rate correction.

THEORY

To assess the TPF for conventional SEC, two aspects need to be investigated:

- o the error in measured flow rate;
- o the effect of this error on the molecular weight averages and the molecular weight distribution.

The second mentioned point is related to the need for flow rate correction which is the whole motivation for the work. The next section examines this need. Following that, the topic of determining the error in measured flow rate is discussed. Finally, quantitative estimation of the error propagation of the flow rate error through to the final molecular weight averages and molecular weight distribution is described.

Assessment of the Need for Flow Rate Correction

The need for flow rate correction depends upon the quantitative information required, the SEC hardware and the type as well as magnitude of flow rate variations present in the system. In "standard" SEC only one detector, a differential refractometer is present. Molecular weight distributions and molecular weight averages can readily be calculated for linear homopolymers. Large changes in flow rate can influence polymer fractionation (12). However, most often only small errors are involved. Assuming small changes, the influence of flow rate error is mainly that it introduces an error into the retention volume calculated from the product of flow rate and retention time. True retention volume for a specified molecular size is expected to be a constant. When flow rate varies then different retention volume values will be calculated. Considering the chromatogram of a polydisperse sample injected into a standard SEC with only a single refractometer detector, the consequence of an error in retention volume is that an incorrect molecular weight will be assigned to each point. As evident from the published literature (3, 13-18) that this error can be quite large particularly if flow rate "drifts" during a run or from run to run (13). Random fluctuations of flow rate within a run are considered of lesser importance. Chamberlin and Tuinstra (3) estimate that at least a 0.5% precision in retention volume **measurement** is necessary to obtain a precision in derived molecular weight of 5% at each retention volume. However, using error propagation analysis, Balke (18) pointed out that the error in molecular weight depended upon both the error in retention volume and the actual value of the retention volume involved. The slope of the calibration curve is important.

Avoiding the use of retention volumes and instead retaining only retention times does not solve the problem. Variations in flow rate will result in different retention times for the same sample. Error analysis could be done on this basis. However, with modern detectors, interpretation centers about retention volume. Therefore, in this paper we will assume that retention volume rather than retention time is to be utilized. All of the subsequent development is based upon this convention.

For SEC utilizing Low Angle Laser Light Scattering (LALLS) or Differential Viscometer (DV) detectors an absolute value of concentration in each retention volume increment is required. The calculated concentration actually depends upon the absolute magnitude of this retention volume increment. Since this volume increment is in turn the product of flow rate and the retention time increment, it can readily be shown (19,20) that the percent error in flow rate will cause the same percent error in concentration. This will result in the same percent error for whole polymer weight average molecular weight from LALLS, for whole polymer intrinsic viscosity from the DV, for local weight average molecular weight from LALLS (i.e. the weight average molecular weight in the detector cell at any time) or local intrinsic viscosity from DV. Considering that flow rate variations in SEC are often less than 1%, the impact of flow rate on these values does not appear very significant.
However, it should be noted that when local properties are plotted versus an erroneous retention volume, very significant errors can be introduced if such plots are used as calibration curves to calculate other averages (e.g. number average molecular weight). This is similar to the effect of flow rate on calibration curves mentioned in the first paragraph of this section. Flow rate effects and interdetector volume for these advanced detectors are two very fundamental concerns that will be the subject of later papers (19,20,21).

Evaluation of TPF Accuracy

Accuracy of the TPF refers to the "closeness to truth" of the flow rate estimate it provides. The TPF is not an absolute instrument. It must be calibrated. Thus, an accuracy study actually is concerned with the stability of this calibration curve with time and with whether the calibration curve is independent of the nature of the mobile phase. Only the second mentioned aspect was examined in this relatively short duration study. Miller and Small (2) found the TPF calibration curve to be independent of the nature of the mobile phase for many solvents. Solvents examined included acetone, tetrahydrofuran and toluene. A theoretical development by Amy and DeWitt (10) shows that a lumped-capacitance source model of the TPF predicts no effect of fluid properties if the TPF calibration curve is linear. In that same work, an apparently less applicable "diffusive-convective" model predicted a strong dependence upon the thermal conductivity of the fluid. In an experimental study of different TPF instruments Macko et al. (11) did see some significant differences amongst various organic solvents and attributed them to differences in specific heat and thermal conductivity.

Evaluation of TPF Precision

Precision of the TPF refers to its "repeatability". This is quantified by determination of the variance. A distinction should be made here with respect to the importance of precision and accuracy. Although short term fluctuations in flow rate are probably not as important to the final calculated SEC results as flow rate drift (inaccuracy) during a run or between runs, to define this drift we need to be able to specify flow rate with small error (i.e. high precision) at each retention time. Thus, the flow meter precision is of direct relevance to its utility and that precision must be distinguished from the variation of the flowrate being monitored.

For pulse transport time data the total variance, s_{tp}^2, is estimated from:

$$s_{tp}^2 = \frac{\Sigma (t_{p,i} - \overline{t}_p)^2}{n - 1} \tag{1}$$

where $t_{p,i}$ is the recorded pulse time at retention time $t_{R,i}$, $\overline{t}_p$ is the average pulse time over the n data points recorded for the run. In this paper, Σ symbolizes a summation over i=1 to n.

This total variance consists of two components:

$$s_{tp}^2 = s_{tp,Q}^2 + s_{tp,TPF}^2 \tag{2}$$

where $s_{tp,Q}^2$ is the contribution to the total variance (s_{tp}^2) due to variations in flow rate and $s_{tp,TPF}^2$ is the contribution of error in the TPF itself.

To examine the variance in flow rate we first change the pulse times to flow rates using the TPF calibration curve. In general, the TPF calibration curve is given by (19):

$$t = A + \frac{B}{Q} + \frac{C}{Q^2} \tag{3}$$

Now the total variance in measured flow rate, s_Q^2, can be calculated from:

$$s_Q^2 = \frac{\Sigma\,(Q_i - \overline{Q}_i)^2}{n - 1} \qquad (4)$$

where Q_i is the flow rate calculated from $t_{p,i}$, and $\overline{Q}_i$ is the mean flow rate.

This also can be considered to be the sum of two variances:

$$s_Q^2 = s_{Q,Q}^2 + s_{Q,TPF}^2 \qquad (5)$$

where $s_{Q,Q}^2$ is the contribution to the total variance s_Q^2 due to variations in flow rate and $s_{Q,TPF}^2$ is the contribution due to error in the TPF itself.

s_Q^2 can also be estimated by using error propagation analysis. Applying the error propagation equation (18,22) to the TPF calibration curve (Equation 3) gives:

$$s_{tp}^2 = ((-B/Q^2) + (-2\ C/Q^3))^2\ s_Q^2 \qquad (6)$$

so,

$$s_Q^2 = s_{tp}^2/((-B/Q^2) + (-2\ C/Q^3))^2 \qquad (7)$$

In assessing the flowmeter, the variance of particular interest is $s_{Q,TPF}^2$ because it is that variance which shows the TPF error in its measured flow rate. We can obtain it from Equation 5 if we know s_Q^2 and $s_{Q,Q}^2$. s_Q^2 can be obtained by either directly calculating it from the flow rate versus time data using Equation 4 or it can be estimated from application of Equations 7. Determination of $s_{Q,Q}^2$ was done here by conducting a special bench scale experiment with the flow meter where the flowrate of the liquid entering the meter was carefully monitored by an independent method. In this experiment the TPF was attached to a high precision syringe pump monitored by a displacement meter. Flow rate was obtained by fitting a plot of syringe displacement expressed as volume displaced versus pumping time. The equation used is:

$$(V - \overline{V}) = Q\ (t - \overline{t}) \qquad (8)$$

where V is the volume displaced, $\overline{V}$ is the average volume displaced over the whole run, Q is flow rate, t is the time required for the run and $\overline{t}$ the average of all the time readings. Equation 8 is essentially a fit of V versus t where the data has been centered about the mean time and mean volume in order to obtain a line with a zero intercept.

The slope was the measured flow rate and its variance ($s_{Q,syringe}^2$) was obtained from the linear regression as:

$$s_{Q,\,syringe}^2 = (\ \Sigma\ (V_i - \overline{V})^2 - (Q\ \ \Sigma\ (t_i - \overline{t})(V_i - \overline{V}))) \ / \ (n-1)\ \Sigma\ (t_i - \overline{t}) \qquad (9)$$

This variance was considered to be the sum of the error due to the random variation of flow rate from the syringe pump ($s_{Q,Q}^2$) and to the displacement meter reading error ($s_{Q,DM}^2$, a quantity which could be independently estimated).

Thus, the variance in flow rate entering the TPF was estimated at:

$$s_{Q,Q}^2 = s_{Q,\,syringe}^2 - s_{Q,DM}^2 \qquad (10)$$

Thus, finally the variance of interest, $s_{Q,TPF}^2$, could be calculated from Equation 5 since both s_Q^2 and $s_{Q,Q}^2$ are known.

Correcting SEC Data Using the TPF

The internal standard method is commonly used in SEC to correct for flow rate variations (18). The strength of this method is that it can effectively correct for changes in flow rate which occur between runs. However, variations which occur within a given run are not taken into account. Also, impurity peak interference or interference with the polymer peak can be troublesome sources of error. The TPF enables flow rate to be monitored every few seconds over the entire course of the analysis.

One way of using the TPF output to correct the retention volume is to integrate the measured flow rate over retention time up to the retention time of interest. This provides a direct measure of retention volume:

$$v = \int_o^{t_R} Q(t)\,dt \qquad (11)$$

An alternative method is to calculate the average flow rate up to the retention time of interest and to use that value to obtain the retention volume at that particular time. This is actually identical to the previous procedure:

$$\bar{Q} = \Sigma\, Q_i\,/n \qquad (12)$$

$$= \Delta t\ \Sigma\, Q_i\,/\,(\,\Delta\, t\, n\,) \qquad (13)$$

$$= \ \Sigma\, Q_i\,\Delta\, t/\,(\,\Sigma\Delta\, t\,) \qquad (14)$$

$$= \int_o^{t_R} Q(t)\,dt/\,t_R \qquad (15)$$

Then

$$v = \bar{Q}\,t_R = \int_o^{t_R} Q(t)\,dt \qquad (16)$$

Finally, we may simply calculate the average flow rate up to the last retention time and utilize that value of flow rate in computing retention volume at each retention time. This is actually the same as the internal standard method and does not correct for flow rate variations within the run.

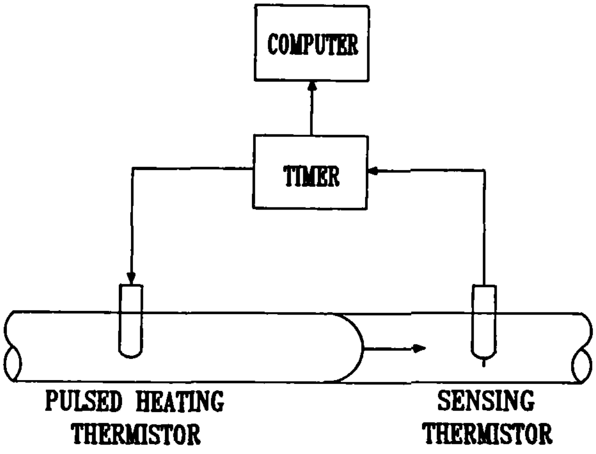

Figure 1: Schematic diagram of the thermal pulse flowmeter (TPF).

In this work we utilized Equation 11 to obtain the corrected retention volumes. Then the usual equations were used to determine the molecular weight distribution and the molecular weight averages.

A practical check on the utility of the TPF is to examine the molecular weight averages before and after flow rate correction. Replicate injections of the same sample are made. The average value obtained for each molecular weight average of interest and its standard deviation are calculated. The normalized (unit area) chromatograms before and after correction are also examined.

If the TPF is working without error then the reproducibility of the corrected values would be expected to be at least equal to the reproducibility of the uncorrected values. If flow rate is the source of imprecision then improvement would be expected. Chamberlin and Tuinstra (3) examined this aspect for a broad polystyrene standard. The precision of molecular weight averages appeared to improve after correction. For example, the standard deviation for weight average molecular weight, M_w, was 2.9% before correction and 1.9% afterwards. Molecular weight distributions superimposed after correction even when they were strongly displaced by flow rate variations before correction. The details of the TPF design can be very important to such a result. For example, Macko et al. (11) determined that an early version of the TPF they examined provided only a 1.16% error standard deviation in measured flow rate whereas a more recent version showed 0.14% error standard deviation.

The same considerations are also present with regards to accuracy. If flow rate is a source of inaccuracy then use of the TPF would be expected to cause the average of the corrected values to more closely approach the true value for the standard.

EXPERIMENTAL

Evaluation of TPF Accuracy and Precision

A Molytek Inc. (Pittsburgh, PA) stainless steel - high pressure flow cell was connected to an ISCO LC-2600 syringe pump operating at room temperature using .009 in. I.D. stainless steel tubing. A Heidenhain VRZ 403 Displacement meter was attached to the syringe pump to record the flowrate from the pump. A Thermalpulse II flowmeter control unit was used to interface the flowcell with a micro-computer for data acquisition (Figure 2). Pulse times were recorded from the flowmeter using the RS-232 communication port. Three solvents were used for the evaluation of the flowcell: HPLC grade tetrahydrofuran, toluene, and acetone. Flowrates ranging from 0.3 to 1.6 mL/min. were pumped through the flowcell. The mass of the solvent accumulated was also recorded using an electronic balance and compared to that recorded by the displacement meter. However, the electronic balance data was used only as an approximate check on the performance of the system and is not reported here.

High Temperature Size Exclusion Chromatography

A Waters model 150C high temperature size exclusion chromatograph was used with 1,2,4-trichlorobenzene (TCB) at 145°C as the mobile phase at 1 mL/min. Three 10 micron PLgel (Polymer Laboratories, Inc.) columns consisting of a 1.0E06 pore size and 2 mixed beds were used for polymer fractionation. Monodisperse polystyrene (Toyo Soda Manufacturing Co., Ltd, Tokyo, Japan) and polydisperse polystyrene (American Polymer Standards) standards were injected at 0.2 wt% and 200 μL. A Molytek stainless steel - high pressure flow cell was installed on-line on the 150C following the refractometer. A Thermalpulse II flowmeter control unit was used to collect pulse times from the flow cell. A micro-computer was used to collect both the refractometer response from the 150C and the flowmeter pulse time.

RESULTS AND DISCUSSION

Evaluation of TPF Accuracy

Figure 3 shows TPF calibration curves for tetrahydrofuran (thf), toluene and acetone determined for the syringe pump experiment. Straight lines were obtained. However, the calibration curves all appear quite different, especially the curve for acetone. Properties such as thermal conductivity, specific heat, density and viscosity for acetone were much different from the other two solvents. According to these results, to obtain good accuracy it is necessary to recalibrate the TPF when solvents are changed.

Evaluation of TPF Precision

Figures 4 and 5 show the recorded pulse transport times as a function of run time for thf and toluene respectively. Figures 6 and 7 show the corresponding plots

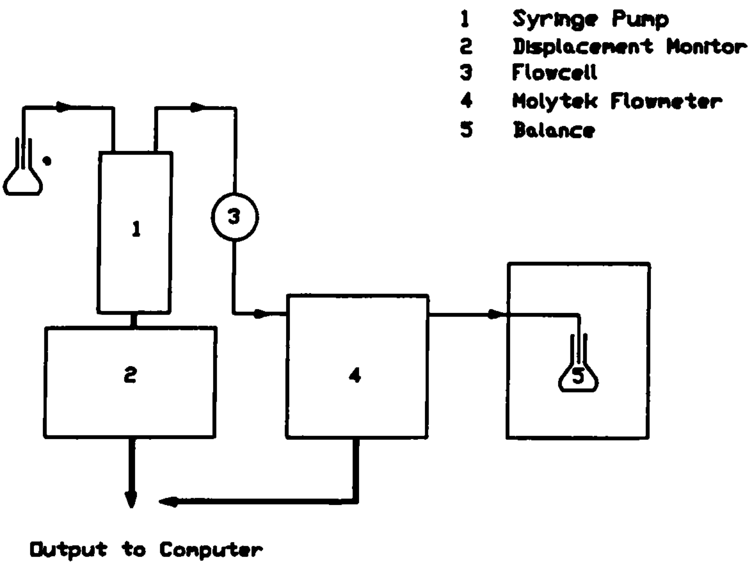

Figure 2: Schematic diagram of the system used to evaluate TPF accuracy and precision.

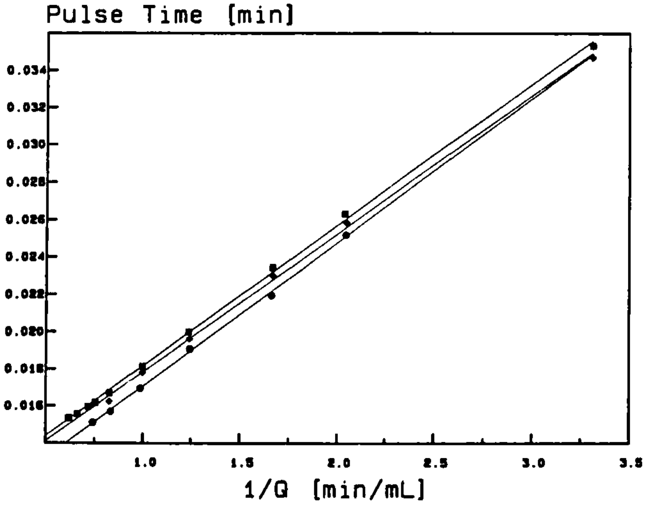

Figure 3: TPF calibration curves:

- ◆ tetrahydrofuran (THF)
- ● acetone
- ■ toluene

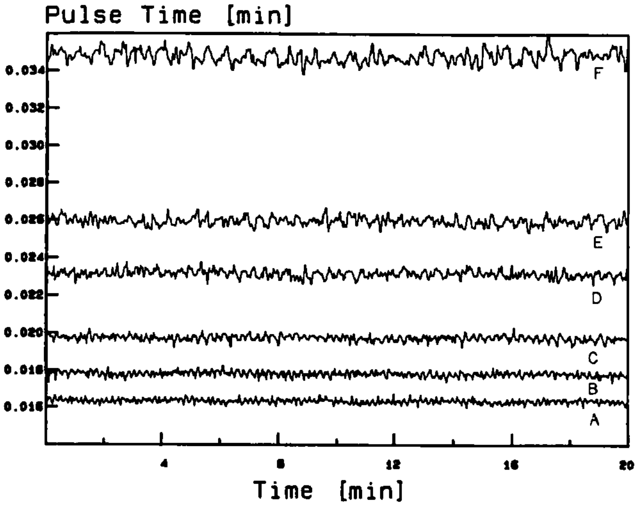

Figure 4: Pulse transport time variation with run time for THF. Letters indicate nominal flow rate settings: A: 1.2 cc/min; B: 1.0 cc/min; C: 0.8 cc/min; D: 0.6 cc/min.; E: 0.5 cc/min; F: 0.3 cc/min.

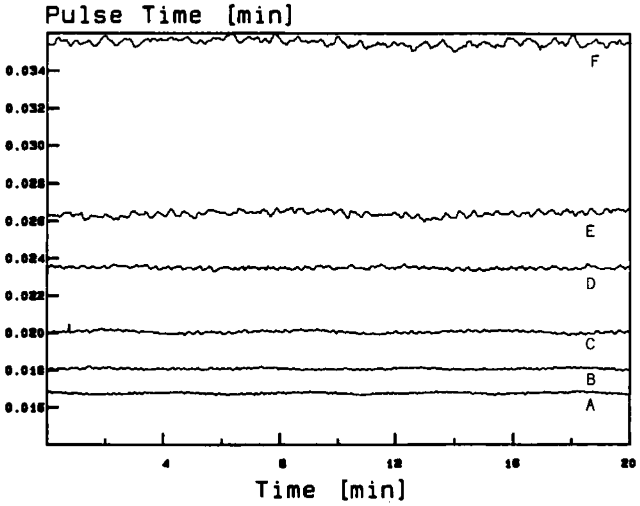

Figure 5: Pulse transport time variation with run time for toluene. Letters indicate nominal flow rate settings: A: 1.2 cc/min; B: 1.0 cc/min; C: 0.8 cc/min; D: 0.6 cc/min.; E: 0.5 cc/min; F: 0.3 cc/min.

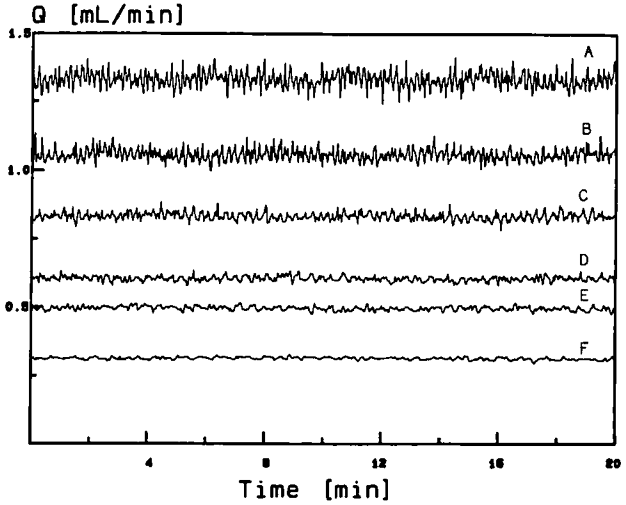

Figure 6: Flow rate variation with run time for THF. Letters indicate nominal flow rate settings: A: 1.2 cc/min; B: 1.0 cc/min; C: 0.8 cc/min; D: 0.6 cc/min.; E: 0.5 cc/min; F: 0.3 cc/min.

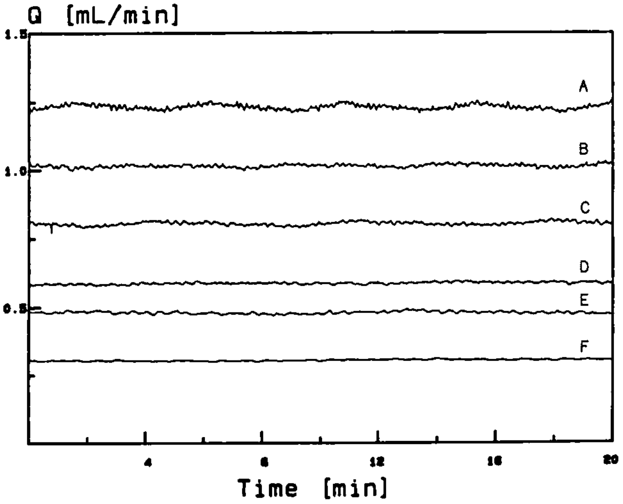

Figure 7: Flow rate variation with run time for toluene. Letters indicate nominal flow rate settings: A: 1.2 cc/min; B: 1.0 cc/min; C: 0.8 cc/min; D: 0.6 cc/min.; E: 0.5 cc/min; F: 0.3 cc/min.

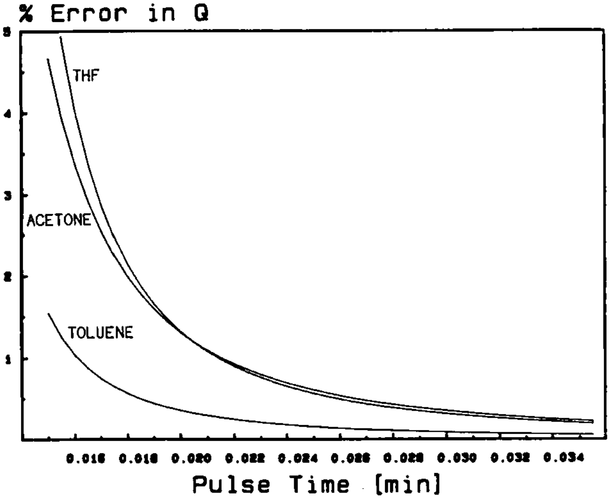

Figure 8: Variation of % error in flow rate with pulse transport time for a s_{tp}^2 corresponding to a flow rate of 1 ml/min for THF, acetone and toluene.

of flow rate versus run time. There is random noise evident in all of the data. In the pulse time data this noise becomes worse as pulse transport times become greater. In the flow rate data the noise becomes worse at higher flow rates (lower pulse transport times). Error propagation analysis using Equation 7 leads us to expect the flow rate to be more sensitive to noise in the pulse transport time at low values of this time. Figure 8 calculated using this equation shows the percent error in flow rate as a function of pulse transport time for a s_{tp}^2 corresponding to a flow rate of 1 cc/min. and clearly shows this sensitivity.

Tables I and II summarize the variance values calculated in the work for thf and toluene. In agreement with Figures 4 and 5 the variance values for the pulse transport times (s_{tp}^2) are seen to increase as flow rates decrease (i.e. as pulse transport times increase). In agreement with Figures 6 and 7 the variance values for the flow rates (s_Q^2 from Equation 4) decrease as flow rate decreases. Values of s_Q^2 calculated using error propagation (Equation 7) are also shown. They agree very well with those directly calculated from the data using Equation 4. The variance $s_{Q,Q}^2$ (the contribution of flow rate to the variance calculated from the displacement meter) were obtained by applying Equation 9 to plots of (V_i - $\overline{V}$) versus (t_i - $\overline{t}$) to obtain $s_{Q,syringe}^2$. Figures 9 shows a typical plot. All such plots showed extremely small amounts of random noise and consequently values of $s_{Q,syringe}^2$ were very small. Furthermore, $s_{Q,DM}^2$, the error contribution of the displacement meter was considered negligible. Thus from Equation 10, $s_{Q,syringe}^2$ was equal to $s_{Q,Q}^2$. What all this meant was that the noise recorded by the displacement meter was probably the actual variation of flow rate entering the TPF. The main uncertainty in this result was the possibility of

TABLE I

ANALYSIS OF SYRINGE PUMP DATA: TETRAHYDROFURAN

Q	s_{tp}^2	s_{QQ}^2	s_Q^2 Eqn.7	s_Q^2 Eqn. 4	$s_{Q,TPF}^2$	100 $s_{Q,TPF}/Q$
cc/min.	min^2	- - - - - - -	(cc/min)^2	- - - - - - -	- -	%
	x 10^8	x 10^9	x 10^4	x 10^4	x 10^2	
1.2147	1.7122	1.5418	6.7803	7.8482	2.8015	2.3
1.0058	2.3863	4.9672	4.4424	4.5440	2.1317	2.1
0.8083	2.6653	1.9204	2.0693	1.9943	1.4122	1.7
0.6008	4.3478	3.7633	1.0305	0.9196	0.9589	1.6
0.4897	6.0344	0.1605	0.6312	0.5748	0.7582	1.5
0.3027	13.3705	0.8910	0.2043	0.2089	0.4571	1.5

TABLE II

ANALYSIS OF SYRINGE PUMP DATA: TOLUENE

Q	s_{tp}^2	s_{QQ}^2	s_Q^2 Eqn. 7	s_Q^2 Eqn. 4	$s_{Q,TPF}^2$	100 $s_{Q,TPF}/Q$
cc/min.	min^2	- - - - - - -	(cc/min)^2	- - - - - - -	- -	%
	x 10^9	x 10^9	x 10^5	x 10^5	x 10^3	
1.2120	2.3123	2.0154	8.7581	9.3536	9.6713	0.8
1.0052	1.9127	3.9598	3.4272	3.5216	5.9340	0.6
0.8109	5.7757	1.5523	4.3828	4.1814	6.4663	0.8
0.6016	5.4840	1.3127	1.2609	1.1419	3.3790	0.6
0.4919	23.7695	1.6386	2.4420	2.1961	4.6861	1.0
0.3025	31.1636	0.8497	0.4582	0.4639	2.1536	0.7

some type of damping in the displacement meter. An assumption in our interpretation is that this damping was of negligible importance. With this interpretation, as shown in Table I the precision of the TPF varies from 0.6 to 2.3% in measured flow rate.

In addition to the random error, there was a barely discernible oscillation with a period of approximately 8 min. in pulse time data for the low pulse times. The corresponding high flow rate data in Figures 6 and 7 show the oscillation more clearly. To examine this and to see a magnified view of the noise in the displacement meter a plot of residuals is shown in Figure 10. Residuals were defined as $(V_i - \overline{V})_{experimental} - (V_i - \overline{V})_{fitted\ line}$. The oscillation in Figure 10 has the same period as that shown in the high flow rate data of Figure 7. That is strong evidence that it is the flow rate from the syringe pump and not the TPF which is the source of the oscillations.

Correcting SEC Data Using the TPF

Figure 11 shows the TPF calibration curve for TCB in the high temperature SEC. Again a straight line was obtained but again this was a different straight line than any previous room temperature ones obtained with the syringe pump system. Figure 12 shows the percent error in flow rate as a function of pulse time applicable to our SEC runs. Pulse times for these runs were approximately 0.020 min. As is evident from this figure, at this point the meter is beginning to be very sensitive to the value of pulse time.

Figures 12 and 13 show the normalized chromatograms for the six replicated samples before and after flow rate correction respectively. Although the curves overlap well in both figures there is a somewhat high level of random noise in the detector response. Shortly after the study, column resolution drastically deteriorated and the columns required replacement.

Table III shows the result of correcting the molecular weight averages for flow rate using the TPF. Average flow rate for each run is also shown. The flow rate correction improved accuracy of M_n. However, accuracy of M_w and precision of both M_n and M_w apparently were slightly worsened.

CONCLUSIONS

- The TPF is an elegant device for measuring flow in SEC throughout the run. The main difficulty in evaluating it is that its error level is of a very small magnitude. It became increasingly evident in the study that SEC results themselves, being highly sensitive to flowrate, likely provide the best method of evaluation.

- The calibration curves for the TPF were straight lines but were found to vary with the type of solvent used.

- A method of using a syringe pump to evaluate the precision of the flowmeter was developed. Single standard deviation precisions ranging from 0.6 to 2.3% in measured flow rate were obtained. These values may be biased high if the

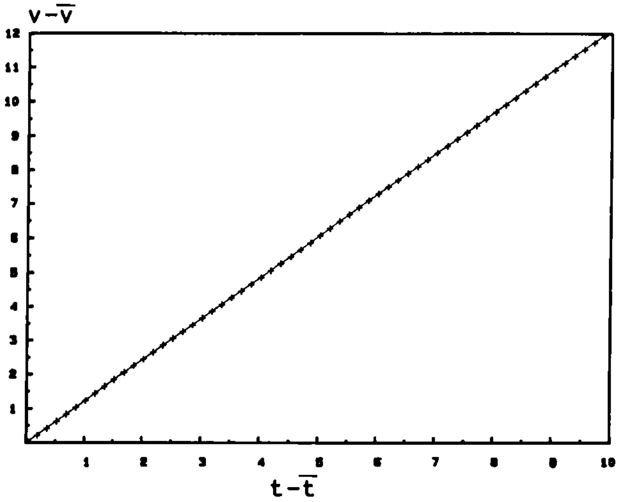

Figure 9: Plot of displacement meter data for toluene at 1 ml/min.

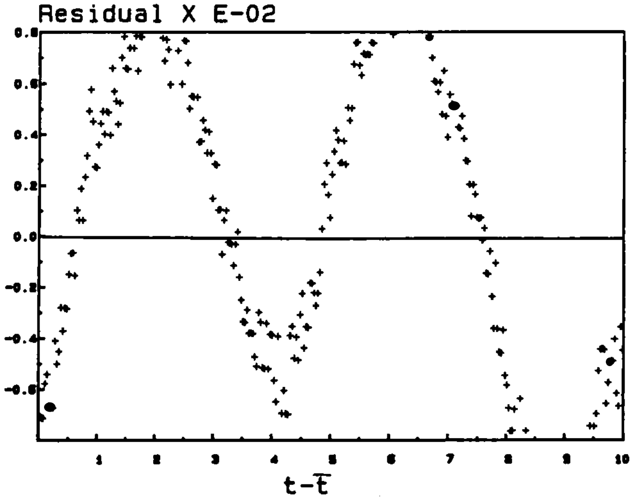

Figure 10: Plot of residuals for Figure 9.

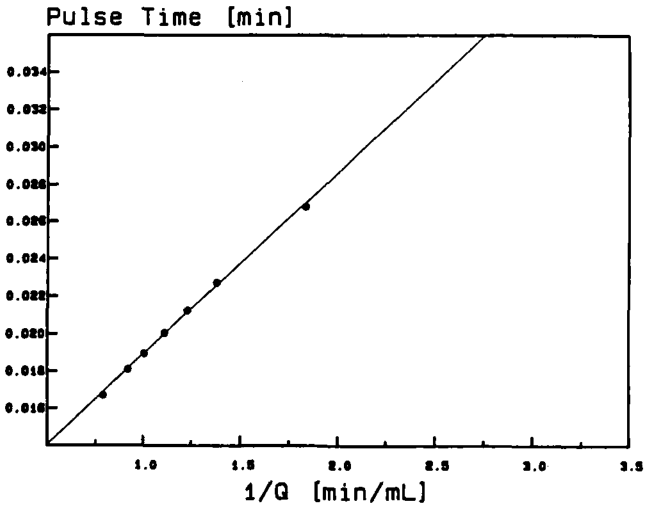

Figure 11: TPF calibration for 1,2,4 trichlorobenzene in the high temperature SEC.

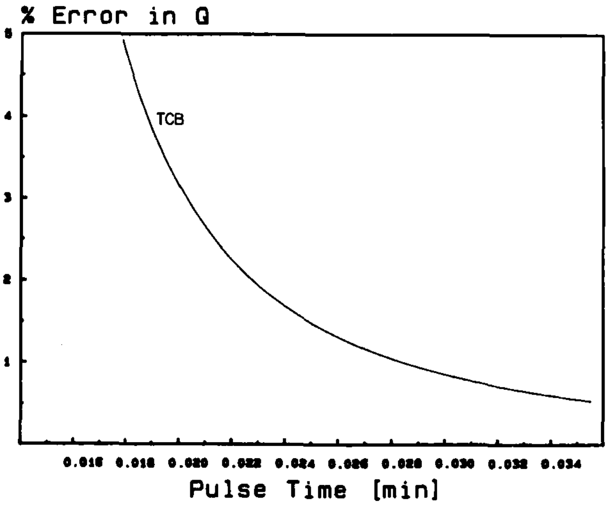

Figure 12: Variation of % error in flow rate with pulse transport time for 1,2,4 trichlorobenzene for a s_{tp}^2 corresponding to a flow rate of 1 ml/min.

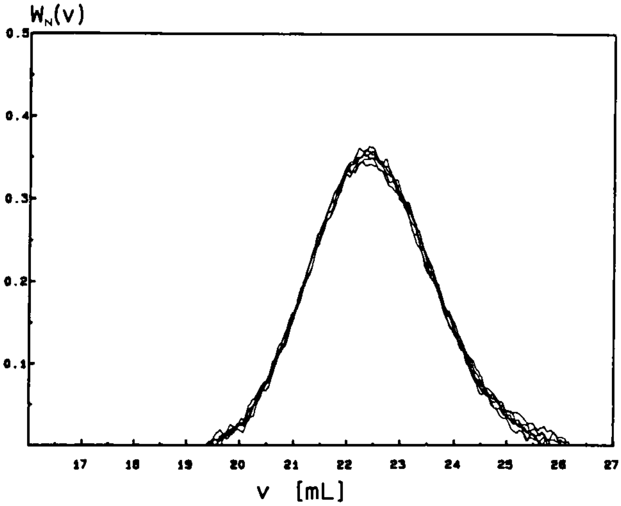

Figure 13: Normalized chromatograms of six replicates of a broad molecular weight distribution polystyrene standard before flow rate correction.

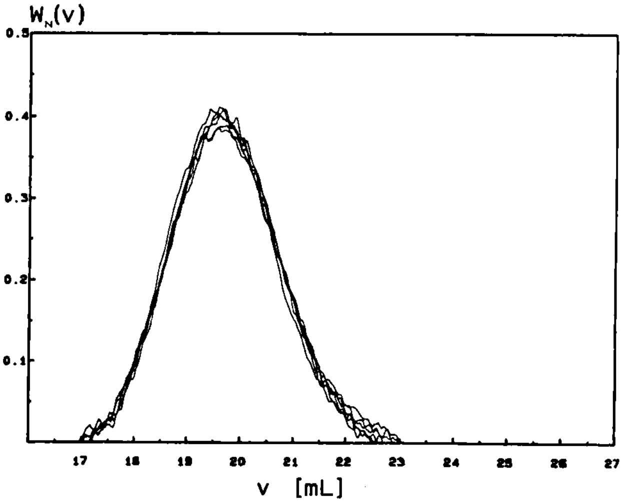

Figure 14: Normalized chromatograms of Figure 13 after flow rate correction using the TPF data in Equation 11.

TABLE III

CORRECTION OF MOLECULAR WEIGHT AVERAGES USING THE THERMAL PULSE FLOWMETER

SAMPLE	$M_n(uQ)^*$ x 10^{-3}	$M_n(cQ)^*$ x 10^{-3}	$M_w(uQ)^*$ x 10^{-3}	$M_w(cQ)^*$ x 10^{-3}	Q cc/min.
True Values	95.0	95.0	235.	235.	
1	113.	111.	232.	236.	0.8780
2	103.	91.5	231.	218.	0.8959
3	96.1	85.7	226.	216.	0.8975
4	106.	102.	223.	216.	0.8769
5	114.	103.	233.	223.	0.8908
6	104.	94.	229.	217.	0.8836
MEAN	106.	97.9	229.	221.	0.8871
STANDARD DEVIATION (S.D.)	6.69	9.16	3.85	7.80	0.00893
100 S.D. / MEAN	6.31	9.36	1.68	3.53	1.01
ACCURACY = 100 (TRUE - AVG.) / TRUE	11.6	3.1	2.6	5.9	---

*Note:
uQ means uncorrected for flow rate
cQ means corrected for flow rate using the TPF and Equation 11.

displacement meter used with the syringe pump has significant damping. Also, systematic variations in the measured flow rate were shown to be true flow variations due to the syringe pump and not the flow meter.

- As mentioned above, SEC results provide the most practical method of evaluating the flow meter. Examining both accuracy and reproducibility of molecular weight averages before and after flow correction is involved. In our system, flow correction significantly improved accuracy of M_n but may have slightly worsened accuracy of M_w as well as precision of both averages. Chromatograms appeared to have the same reproducibility before and after correction. However, in both cases, chromatogram noise was greater than normal probably because of column degradation problems.
- Error propagation analysis was shown to provide a simple method of relating error in flow rate to error in the pulse transport time. Error in measured flow rate is larger at lower pulse transport times.

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