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Short communication

Experimental method to distinguish column dead time from system dead time for the accurate determination of gas chromatographic void volumes: simultaneous pre- and post-column injection

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Abstract

A new experimental technique for the accurate determination of the dead time of a chromatographic column is described. The technique involves simultaneous pre- and post-column injections of an unretained probe solute. The method allows the accurate determination of the *column* void volume as opposed to the *system* void volume which includes extracolumn volumes. The procedure also eliminates the uncertainties in void volume measurements caused by splitters, multiple flow paths, or auxiliary gas flows required for some detectors or certain types of chromatography such as supercritical fluid chromatography.

1. Introduction

Accurate measurement of the dead time and hence the void volume of a chromatographic column is critical to the experimental determination of thermodynamic parameters from any chromatographic experiment. The problem is very complex and troublesome as evidenced by the multitude of discussions and reviews in the literature [1–10]. Moreover, most of these papers cite multiple prior studies: Kazakevich and McNair [8] for example cite 28 previous investigations involving different methods for the evaluation and definition of the void volume of chromatographic columns in liquid and gas chromatography.

Currently, there are at least four commonly used strategies for measuring this critical parameter, viz., (i) gravimetric determination of the weight of mobile phase of known density in a column, (ii) selection of a dead time which gives the "best" linear fit for a plot of the log of the adjusted retention time of a homologous series of solutes vs. carbon number or some other linearization parameter, (iii) measurement of the retention volume of a dead time probe solute *which is unretained and unexcluded by the stationary phase*, and (iv) measurement of the retention times of isotopically labeled components of the mobile phase or system peaks.

In addition to the experimental difficulties, the exact definition of the void volume is often ambiguous especially for liquid systems in which the mobile phase may solvate the stationary

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phase, as well as low-temperature GC or high-pressure SFC systems in which the stationary phase may consist primarily of adsorbed components of the mobile phase. RP-HPLC with alkane-bonded stationary phases also presents conceptual problems because of the uncertain role of the bonded phase in the retention mechanism(s). In such cases, precise definition as well as accurate measurement of the void volume is imperative before any meaningful thermodynamic measurements can be reported or interpreted.

Accurate void volume measurements are particularly difficult if the flow stream of the mobile phase is split or augmented at some point in the apparatus. Inlet splitters are common with capillary GC systems, outlet splitters are sometimes used with mass specific detectors, and other detectors require a makeup gas. Some more complex multidimensional chromatography instruments [11,12] use multiple columns with makeup gas or flow splitting for each column. These configurations with variable flow paths and rates exacerbate the difficulties of accurately measuring the void volume of a given column.

In the present work, a new experimental technique for the determination of void volumes using strategy iii is described. The method involves the injection of the same sample simultaneously at the inlet and outlet of the analytical column. The dead time of the column is obtained from the residence time of the dead time probe *between the two injection sites*, i.e., in the column not the extracolumn plumbing or the detector.

2. Experimental

A simplified schematic diagram of the dual injection technique is illustrated in Fig. 1 for a typical system with a detection system which requires a splitter or auxiliary gas. Pneumatically actuated valves Nos. 1 and 2 are switched simultaneously to provide two sample pulses, only one of which passes through the analytical column. The sample injected via valve No. 2 remains undifferentiated and serves only as a marker for the residence time of any solute in the extracolumn regions of the instrument. This residence time may be influenced by the split ratio if a splitter is used or by the flow-rate of the auxiliary or makeup gas if the detector requires such flows. In any case, the extracolumn residence times of the samples injected from both valves will be the same and can be factored out of the column dead time measurements.

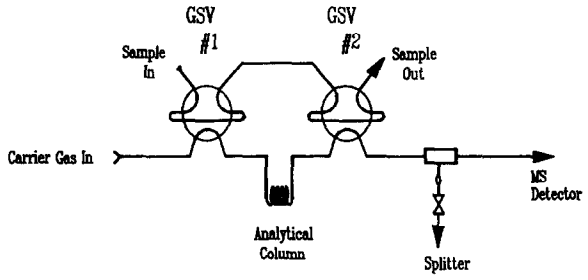

Fig. 1. Schematic diagram of a dual injection system with an outlet splitter. GSV = Gas sampling valve.

3. Results and discussion

A typical chromatogram [13] obtained with a GC–MS system configured as shown in Fig. 1 is given in Fig. 2. Each line in the drawing represents the detector response for a different solute in a carrier gas composed of natural helium, ^{4}He. The mass selective detector was used to monitor various m/z values, viz., $m/z = 3$ for the dead time probe, ^{3}He, $m/z = 20$ for neon and $m/z = 47$ for isotopically labeled carbon dioxide. The first peaks in the chromatogram are due to the coelution of all of the sample components injected from sampling valve No. 2. The retention time of these samples gives the residence time of any solute in the extracolumn segments of the system. The time from injection to elution of the dead time probe injected from valve No. 1 is the dead time of the entire system. Whereas, the difference between the elution time of the ^{3}He probe injected from valve No. 1 and that injected from valve No. 2 gives an accurate measure of the dead time of the analytical column.

Such an instrument has been used to measure very small changes in the measured void volume of a gas–solid chromatographic column as a

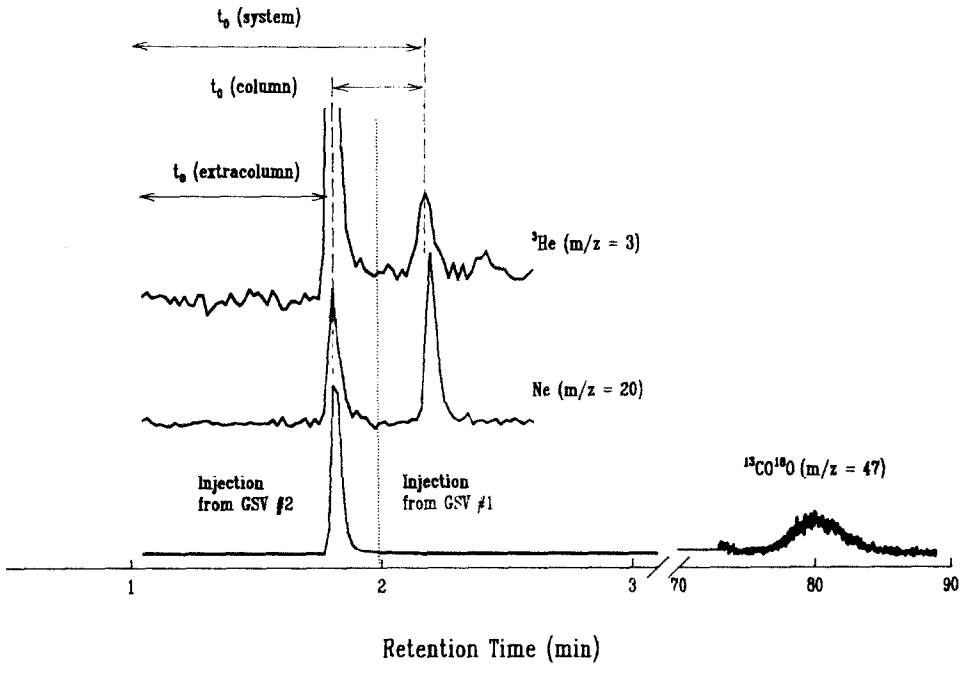

Fig. 2. Example chromatogram obtained from a dual injection instrument [13]. The solutes were injected simultaneously at both sampling valve at 1 min.

function of the amount of material adsorbed from the mobile phase at low temperatures (77 K) [13]. Fig. 2 represents a typical chromatogram obtained from that investigation involving the adsorption of carbon dioxide on silica gel. In this example, the residence time of the solutes in the extracolumn regions of the flow path was 1.80 min compared to the residence time of the ^{3}He probe in the column of only 0.17 min. That is, if the volume flow-rates were equal in the two regions, the measured extracolumn volume would be approximately ten times as large as the *column* void volume. The proposed dual injection technique allows the extraction of the latter quantity from the much larger *system* void volume and thus small changes in the column dead time and void volume could be accurately measured. The results for carbon dioxide adsorbed at 77 K are shown in Fig. 3. The precision of the measurements is sufficient to allow an accurate measurement of the decrease in void volume with increasing amounts of carbon dioxide adsorbed to give a direct measure of the molar volume of *adsorbed* carbon dioxide. Thus, it was also possible to measure the *volume* of material adsorbed as a function of the relative pressure of adsorbate in the mobile phase to produce a truly "volumetric" isotherm [13].

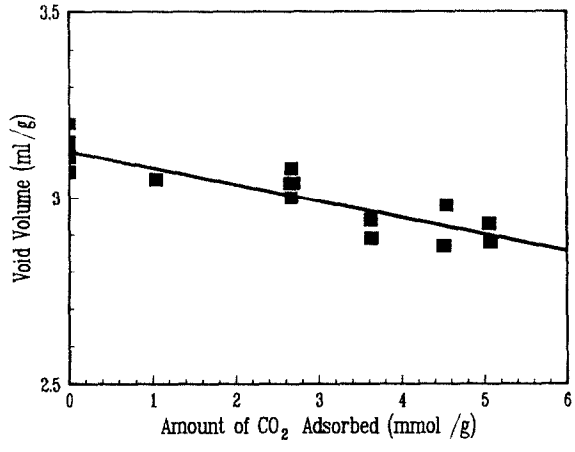

Fig. 3. Void volume measured with dual injection method with various amounts of CO_2 adsorbed on silica gel at 77 K.

4. Conclusions

There are several advantages as well as concomitant disadvantages of the proposed dual injection scheme. Some of the advantages are:

- The technique can be used to distinguish the *column* void volume from the ordinarily much larger and more uncertain *system* void volume.
- Accurate determination of the absolute injection time is not critical. Measurement of a relative retention difference rather than an absolute retention time from injection minimizes the uncertainty from the specification of the exact time of injection. Such uncertainty is especially large for manual syringe injections.
- The technique can be used with any type of chromatography, i.e., GC, SFC, and HPLC.
- The peak profile of the post-column injection peak gives a snapshot of the pre-column injection peak. Thus, changes originating in the column can be distinguished from those occurring in other parts of the system such as the detector. Relevant changes include band spreading, chemical reactions, and isotope exchange processes.

An unforeseen advantage of the dual injection scheme is the fact that the detector response to the sample injected via valve No. 2 gives an undifferentiated profile of the sample injected at valve No. 1. This is especially valuable with a mass specific detector because it provides knowledge of exactly what was injected into the analytical column even if all or part of the sample does not elute in a reasonable time or elutes with the dead time marker.

There are also a number of disadvantages to the proposed method:

- The added complexity and expense of two pneumatically controlled sampling valves may be significant.
- The method still requires a viable dead time probe solute, i.e. a solute which is not retained by the stationary phase.
- Peak overlap may become a limiting problem with non-specific detectors especially for columns with very low void volumes.
- The experimental technique does not eliminate the ambiguities of, or the need for, an exact definition of the void volume and mobile phase volume of a given column.
- Dual injections of a scarce sample is undesirable. This can be overcome by injection of only the dead time marker in the post-column injector; however, some of the advantages cited above will be lost in this case.
- The post-column sampling valve will itself contribute to peak spreading because of its crucial position between the exit of the column and the detector.
- The dual-injection technique is only valuable for instruments in which either the system void volume is significantly larger than the column void volume or there are multiple flow paths for the mobile phase.

The proposed injection scheme will solve some but certainly not all the problems encountered in the accurate assessment or even the exact definition(s) of the void volume and the mobile phase volume of a chromatographic column. In many cases, these two volumes are not equivalent, and extraordinary care must be exercised in the presentation and interpretation of chromatographic retention data and thermodynamic information derived from such data.

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