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Ion-chromatographic analysis of common anions, acetate, and formate in 30% hydrogen peroxide
Statistical evaluation of two automated microbore systems

L.E. Vanatta[a,*], D.E. Coleman[b]

[a]Air Liquide America, Box 650311 MS 301, Dallas, TX 75265, USA
[b]Alcoa Technical Center, MST-D, 100 Technical Drive, Alcoa Center, PA 15069, USA

Abstract

Two hydroxide-selective microbore analytical columns (the Dionex AS11 and AS15) were tested and compared for the quantitation of anionic species in 30% hydrogen peroxide. The ions of interest were fluoride, acetate, formate, chloride, bromide, nitrate, sulfate, and phosphate. Statistically sound calibration and spiking studies were carried out, investigating the range of a blank to 60 ppb. Prior to injection onto the separators, peroxides were loaded without pretreatment onto a concentrator column, which was then washed with deionized water to remove the matrix. Although retention times gradually decreased during the spiking studies, reliable quantitation was still achievable on both columns at the target concentration of 30 ppb. However, various resolution problems meant that the AS11 should not be recommended for this application.
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1. Introduction

A need exists to quantitate anionic species in ultrapure, concentrated hydrogen peroxide (30%, w/w). In the semiconductor industry, the current peroxide specifications restrict most ionic species to no more than 30 ppb (w/w) of each contaminant [1]. Ion chromatography is well suited for determining anions and organic acids. However, 30% H_2O_2 is a difficult matrix, which may attack the column resins, thereby shortening the lifetime of these separators [2].

To address this problem, most past procedures have been based on decomposition of the concentrated peroxide [3,4]. However, this technique is prone to loss of analyte and/or contamination. One group of researchers has improved the approach by designing an on-line decomposer [5], but this apparatus is not commercially available. Three other papers have reported on-line matrix-elimination procedures [6–8]. In all cases, a given volume of 30% H_2O_2 was loaded onto a concentrator column; the matrix was eliminated by washing the resin with water. Subsequently, the retained ions were eluted onto the separator column for chromatography. Kerth et al. [6] used a 4-mm Dionex AS11 separator, and loaded and rinsed the concentrator via a sampling pump. Meissner et al. [7] employed a 4-mm Dionex AS12A separator; presumably, they used a sampling pump, although details are not given. Collard et al. [8] chose a 4-mm Dionex AS15 separator, and loaded and rinsed the concentrator via an auto-

*Corresponding author. Tel.: +1-972-995-7541.
E-mail address: lynn.vanatta@airliquide.com (L.E. Vanatta).

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sampler; in addition, they used a Dionex EG40 Eluent Generator.

No one, though, has investigated or compared any columns in the 2-mm format, which affords the user an increase in sensitivity and a decrease in eluent usage. Therefore, this study evaluates the hydroxide-selective AS11 and AS15 microbore columns. (The AS12A was not chosen because it is carbonate-selective and thus not as sensitive as the other two columns.) In addition, this research is based on a more rigorous and more systematic use of statistics than has been employed in past publications. Such analyses are needed by users to compare methods and decide if the procedures will meet the quality objectives of their project. Comparison of these separators is also needed for a practical reason; the AS15 must be housed in a heated chamber. Side-by-side data will show if the extra expense is required for reliable data.

Because the Eluent Generator is not available in all labs, the EG40 was not used in this current research. An autosampler was used, since: (1) it allows a large volume of sample to be analyzed, (2) it eliminates the need for and maintenance of an extra valve, pump, and water reservoir, and (3) it permits automated sample introduction.

The purposes of this paper are: (1) to evaluate statistically and compare the microbore AS11 and AS15 columns for this automated, matrix-elimination approach to determining anions and organic acids in H_2O_2, and (2) to discuss precautions and recommendations for use of this protocol.

2. Experimental

2.1. Materials

Sodium hydroxide (50%, w/w, with ≤0.10% sodium carbonate) from Fisher Scientific (Pittsburgh, PA, USA) was used to prepare the concentrated eluent solutions of 40 m*M* and 200 m*M*. Stock standards [1000 ppm (w/w) each] of fluoride, chloride, bromide, nitrate, sulfate, and phosphate were secured from Alltech Associates (Deerfield, IL, USA); sodium acetate (99.995%) and sodium formate (99.998%) were purchased from Aldrich (Milwaukee, WI, USA). For eluent preparation and dilution of standards, deionized (DI) water (18 mΩ cm) was delivered by a point-of-use water-purification system (Ionics-Ahlfinger, Dallas, TX, USA). Hydrogen peroxide (30%, containing no additives or stabilizers) was obtained from Air Liquide America (Dallas, TX, USA).

Water for eluents was sparged with helium before use. Subsequently, the DI water (for diluting of eluent concentrates) and the two NaOH reservoirs were kept under pressure with helium throughout their life.

Peroxide test strips from EM Science (Gibbstown, NJ, USA) were used when checks of solutions or waste effluent were desired.

2.2. Apparatus and columns

Unless otherwise noted, all instrument modules and supplies were from Dionex (Sunnyvale, CA, USA). Two DX 500 microbore ion chromatographs were used for all analyses. Analytical columns were: (1) an IonPac AG11 Guard (2 mm×50 mm) with AS11 Analytical (2 mm×250 mm) and (2) an IonPac AG15 Guard (2 mm×50 mm) with AS15 Analytical (2 mm×250 mm). All tubing in the chromatography paths was PEEK (polyether ether ketone) [0.005 in. (0.125 mm) I.D.].

To deliver eluent to the systems, a GP50 Gradient Pump was used for the AG/AS11 columns and a GP40 Gradient Pump was employed for the AG/AS15 set. Gradient programs and flow rates are given in Table 1. For concentrating standards and spikes, each system was equipped with a TAC-LP1

Table 1
Gradient programs for AS11 and AS15 columns

Time (min)	% of Eluent 1	% of Eluent 2	% of Eluent 3
AS11 [a]			
0.0	98.8	1.2	0
2.5	98.8	1.2	0
6.0	97.5	0	2.5
18.0	80.9	0	19.1
AS15 [b]			
0.0	95	5	
5.9	95	5	
6.0	80	20	

[a] Eluent 1: Deionized water. Eluent 2: 40 m*M* NaOH. Eluent 3: 200 m*M* NaOH. Flow rate=0.25 ml/min.

[b] Eluent 1: Deionized water. Eluent 2: 200 m*M* NaOH. Flow rate=0.40 ml/min.

(35 mm×4 mm) concentrator column. Standards and samples were loaded via AS40 Automated Samplers, with one module on each system. PolyVials (5 ml) and plain caps were used with both autosamplers. Before use, all vials were rinsed 20 times with DI water from the tap; each rinsing consisted of filling the vial completely and then pouring out the water.

Post-column eluent suppression was achieved using Anion Self-Regenerating Suppressors (ASRS-Ultra, 2 mm) in the external-water mode; current was 100 mA. For the AS15 system, the suppressor and all columns were housed in an LC25 Chromatography Oven equipped with a ten-port Rheodyne valve; the oven chamber was kept at 31°C.

To maintain constant equilibrium (especially in the AG/AS15 system [9]), water was allowed to flow continuously through the regenerant chambers of the suppressors, even when the chromatographs were not in use. Flow rates (with ASRS current off) were approximately 20 ml/min. CD20 Conductivity Detectors at an output range of 10 μS were used on both systems.

Instrument control and data collection were accomplished using a personal computer and PeakNet software. JMP software (SAS Institute, Cary, NC, USA) was used to carry out statistical calculations.

2.3. Standards preparation

All standards were prepared in new high-density polyethylene (HDPE) narrow-mouth bottles (Nalge Nunc, Rochester, NY, USA). Either 125- or 250-ml containers were used, depending on the volume requirements of the solution.

A mixed stock (100 ml) of acetate and formate (1000 ppm in each anion) was prepared from the dry chemicals. A mixed standard (100 ml) containing 10 ppm of each of the eight desired analytes was prepared from the various 1000-ppm stock standards.

Two types of intermediate standards (250 ml; each solution was 100 ppb in each analyte) were prepared from the 10-ppm solution. The diluent was DI water for the first type of standard and 30% hydrogen peroxide for the second type. Eight working standards (100 ml each of 1.875, 3.75, 7.5, 10, 15, 20, 30, and 40 ppb) were prepared from each of the intermediates, using the corresponding diluent to bring each working standard to final mass. A standard-preparation blank was also prepared for each type of matrix; i.e., several grams of pure matrix was poured out and brought up to final mass with additional matrix. Added to the set of DI-based working standards was a 60-ppb solution. Its inclusion was prompted by two facts: (1) the density of 30% peroxide is 1.11 and (2) all standards were prepared by mass but loaded onto the concentrator by volume. These two statements meant that a greater mass of peroxide-based solutions was loaded than was concentrated for water-based standards. Therefore, adding the 60-ppb standard prevented extrapolation when predicting 40-ppb peroxide-based standards from water-based calibration curves.

To avoid contamination, deliveries of 10-ppm and 100-ppb solutions were accomplished by pouring. These masses were recorded accurately; the final mass was then adjusted to give the desired concentration. Final amounts of diluents were delivered by polyethylene transfer pipets (from Fisher) that were thoroughly rinsed out with and dedicated to the particular matrix (i.e., either DI water or H_2O_2). New transfer pipets were used to deliver the various 1000-ppm solutions.

All masses were determined using a Sartorius BP301S analytical balance (Sartorius, Edgewood, NY, USA) and were recorded to four decimal places. Dilution errors in the daily working standards were estimated by conducting a Monte Carlo simulation. This exercise was based on the upper bound (0.0001 g) on the magnitude of weighing error for the balance. In the simulation, weighing errors were randomly drawn from a Normal distribution with mean equal to zero and standard deviation equal to the upper bound. The distribution of these relative concentration errors was found never to exceed 0.1% relative error, which was considered negligible.

All standards were prepared fresh each day they were to be used. Each day, preparations and analyses were performed in random order. Peak areas (PAs) were used to measure the chromatographs' responses to each anion.

3. Results and discussion

3.1. Initial calibration studies

Before any peroxide analyses were performed, statistically designed calibration experiments were

conducted on both analytical columns, using water-based standards. Prior to the initial studies, new column sets were installed in each system and used only to optimize the chromatography with water-based solutions. For each separator and anion, this calibration work provided: (1) the appropriate model for the calibration curve, (2) the detection limit (DL), and (3) the ±prediction interval (±p.i.). The DLs and ±p.i.s were calculated for $\alpha=\beta=0.025$, where α and β are the nominal probabilities of false positives and negatives, respectively. These data then served as yardsticks for evaluating subsequent results. Besides the common anions of F^-, Cl^-, Br^-, NO_3^-, SO_4^{2-}, and PO_4^{3-}, acetate and formate were chromatographed. These last two analytes were included to see if organic acids could be quantitated, too.

The initial calibration study was designed with two purposes in mind: (1) to be able to quantify ion levels that were as high as 40 ppb (i.e., slightly above the specification limit of 30 ppb) and (2) to be able to detect single-digit concentrations. To achieve the first priority, a 60-ppb standard was chosen as the highest standard. As explained in Section 2.3, this level would account for the peroxide density's effect on the mass loaded on the concentrator. To ensure a low detection limit, a semi-geometric-based design was chosen. The core design was comprised of concentrations of 1.875, 3.75, 7.5, 15, 30, and 60 ppb. Modifications were made by also including a blank, plus 10-, 20-, and 40-ppb standards. The blank and the 10-ppb solution were added to allow detailed modeling at the low end of the concentration range; the 20- and 40-ppb standards were included to effect more precise curve fitting in the area of the current 30-ppb specification for anions. This suite of standards was tested on each of eight separate days, thereby providing 80 data points for each anion on each column. (Two exceptions were fluoride and acetate on the AS11 column. At the 40- and 60-ppb levels, these two peaks merged, thereby making quantitation of each impossible. Therefore, subsequent data discussions in this section will be based on only 64 data points for these two analytes.)

Prior to beginning the calibrations, models were proposed for each anion's curve. Straight lines, using ordinary least squares (OLS) fitting, were postulated for all anions except fluoride; past experience suggested that a quadratic fit would be appropriate for this analyte.

Representative chromatograms of 30-ppb water-based standards are shown in Figs. 1a (AS11) and 1b (AS15). After all standards had been analyzed, the proposed models were tested, using calibration diagnostics discussed in previous papers [10,11]. Statistical analysis of the peak-area data first involved examining the responses for trends; no practically important trends were seen.

For these initial calibration studies, the appropriate models, R^2_{adj}, the detection limits, and the ± prediction intervals at 30 ppb are reported in Table 2. All prediction intervals were considered acceptable. On the AS11, acetate's value of 4.2 was slightly higher than the others, probably because of the acid's incomplete resolution from fluoride.

For monitoring retention-time stability throughout the research, one peak was selected on each column. The analyte chosen was the one whose retention time exhibited the largest average daily range during the

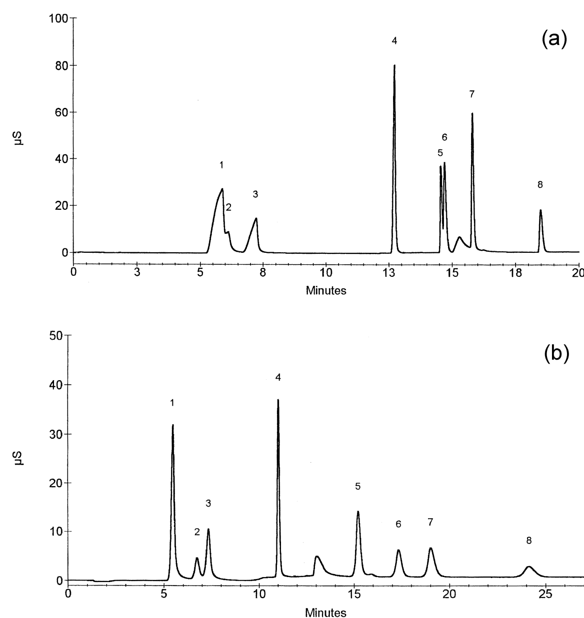

Fig. 1. Example chromatograms of 30-ppb water-based standards on: (a) the AS11 column and (b) the AS15 column. Peak identities on the AS11: (1) fluoride, (2) acetate, (3) formate, (4) chloride, (5) bromide, (6) nitrate, (7) sulfate, and (8) phosphate. Peak identities on the AS15: (1) fluoride, (2) acetate, (3) formate, (4) chloride, (5) sulfate, (6) bromide, (7) nitrate, and (8) phosphate.

Table 2
Results of calibration-study evaluation for AS11 and AS15

Anion	Model[a]	R^2_{adj}	DL (ppb)[b,e]	±p.i.(ppb) at 30 ppb[c]
AS11				
Fluoride	Straight line[d]	0.9994	**0.2**	1.0
Acetate	Quadratic	0.9974	**1.2**	4.2
Formate	Quadratic[d]	0.9959	2.2	2.5
Chloride	Straight line	0.9996	**1.4**	0.8
Bromide	Quadratic	0.9999	**0.7**	0.4
Nitrate	Straight line	0.9993	2.1	1.0
Sulfate	Quadratic[d]	0.9989	**0.6**	1.3
Phosphate	Quadratic	0.9999	**0.8**	0.4
AS15				
Fluoride	Quadratic	0.9997	**1.1**	0.6
Acetate	Quadratic	0.9982	2.5	1.8
Formate	Quadratic	0.9979	3.0	1.8
Chloride	Straight line	0.9995	**1.7**	0.8
Bromide	Straight line	0.9992	2.1	1.0
Nitrate	Straight line[d]	0.9987	**1.2**	1.3
Sulfate	Quadratic	0.9985	3.0	1.4
Phosphate	Straight line	0.9985	2.9	1.4

[a] See Section 3.1 for discussion of model choices.
[b] DL=detection limit, calculated by the method of Hubaux and Vos [10,11]; $\alpha=\beta=0.025$.
[c] ±p.i. at 30 ppb=± prediction limit at 30 ppb; $\alpha=\beta=0.025$.
[d] Weighted least squares (WLS) required for this analyte.
[e] Detection limits that are below the lowest standard of 1.875 ppb have been emboldened.

initial calibration work (range="maximum daily R.T. minus minimum daily R.T."; R.T.=retention time). The ions were chloride on the AS11 and phosphate on the AS15; their average daily ranges were 0.36 and 0.50 min, respectively. Two other statistics were calculated: (1) the shift in the average daily retention time over the course of the study, where the difference was defined to be "final minus initial", and (2) the average relative standard deviation (RSD) for the average daily retention time. In the initial study, the values (in min) for these last two statistics were, respectively: −0.25 and 0.72 for the AS11, and −0.59 and 0.69 for the AS15. These ranges, shifts, and RSDs are included in Tables 3 and 4 for the AS11 and AS15, respectively; these values served as the basis for evaluating stability during the spiking study.

While these calibration standards were being analyzed, data on the reproducibility of the autosamplers were collected. When standards were loaded onto the concentrator columns, waste-line effluents were collected and weighed. For the 80

Table 3
Retention−time statistics for chloride on the AS11 (all values in min)[a]

Study	Average daily range[b]	Shift[c]	Average RSD[d]
Initial calibration	0.36	−0.25	0.72
Spiking (peroxide-based standards)	0.22	−0.49	0.58
Spiking (water-based standards)	0.85	−3.34	2.83

[a] See Sections 3.1 and 3.2.2.3 for details on the ion choice and on the calculations.
[b] Average daily range=average of the daily retention-time ranges, where the range is "maximum daily R.T. minus minimum daily R.T.".
[c] Shift=the shift in the average daily retention time over the course of the study, where the shift is "final minus initial".
[d] Average RSD=the average RSD for the average daily retention time.

Table 4
Retention-time statistics for phosphate on the AS15 (all values in min)[a]

Study	Average daily range[b]	Shift[c]	Average RSD[d]
Initial calibration	0.50	−0.59	0.69
Spiking (peroxide-based standards)	0.40	−3.08	0.65
Spiking (water-based standards)	0.37	−2.98	0.54

[a] See Sections 3.1 and 3.2.2.3 for details on the ion choice and on the calculations.
[b] Average daily range=average of the daily retention-time ranges, where the range is ''maximum daily R.T. minus minimum daily R.T.''.
[c] Shift=the shift in the average daily retention time over the course of the study, where the shift is ''final minus initial''.
[d] Average RSD=the average RSD for the average daily retention time.

determinations on the AS11 and AS15 systems, the averages (±standard deviations) were 5.600 (±0.102) g, and 5.751 (±0.047) g, respectively. For this research, these reproducibilities were considered acceptable enough to consider the volume loaded to be constant throughout.

3.2. Spiking studies

3.2.1. Protocol

A sufficient quantity of 30% peroxide was obtained for use throughout the spiking work. On each day of the study, the working standards (including the blank) were prepared in both DI-water and hydrogen-peroxide matrices, as detailed in Section 2.3. After analysis, the predicted concentrations were calculated for each standard, using the calibration curves developed from the initial calibrations (see Section 3.1). The first set of standards allowed monitoring of the initial calibration curves' predictive abilities. The second suite generated data to test the applicability of water-based curves to peroxide-based samples.

Each day of the study, the following protocol was used. The instruments were activated and equilibrated by analyzing two samples of DI-water, followed by a 30-ppb standard in water. A sample of 30% peroxide, taken directly from the bulk container, was analyzed next, followed by the H_2O_2-based standards and then the water-based standards. As part of another investigation, ten digested-peroxide samples then were analyzed. The final analysis was of the same 30-ppb standard tested at the beginning (i.e., after the two initial DI waters).

3.2.2. Data evaluation

3.2.2.1. Statistical considerations

Evaluation of the ''closeness to true'' often is made by calculating the percent recovery. However, these numbers can be misleadingly large at low concentrations. A better approach, which was utilized in this research, is to calculate the dataset's mean absolute deviation (M.A.D.; the mean of the absolute value of the quantity ''true minus predicted''). These determinations then are compared with the quality objectives of the project. If the M.A.D.s are sufficiently low, then the use of water-based standards is acceptable for generating calibration curves.

For water-based solutions, the above M.A.D. definition sufficed for the calculations. However, the procedure was more complicated for the peroxide-based standards. These solutions were spikes into a matrix that was not background-free in all analytes. The predicted values of interest were those of the spike levels themselves. Therefore, the deviations were calculated daily as follows. First, the predicted concentration of the solution itself was determined, using the appropriate calibration curves (from Section 3.1). Second, these predictions were corrected for the density (1.11) of 30% H_2O_2. Third, the corrected blank prediction for the day was subtracted from each of the eight spikes. Fourth, the eight net concentrations were then subtracted from their respective true levels to determine each deviation. Finally, the M.A.D. for the day was calculated by averaging all eight absolute deviations.

3.2.2.2. Chromatographic observations

Inspection of the peroxide chromatograms (see Figs. 2a and 2b for representative tracings for the AS11 and AS15 columns, respectively) yielded several overall observations on the AS11 column. The front portion (i.e., fluoride through formate zones) of the plots were extremely complicated, making reliable integration virtually impossible. Therefore, no attempt was made to quantify fluoride, acetate, or formate in peroxide on this separator. In addition, bromide and nitrate did not separate well. As a result, the response of one ion depended in part on the concentration of the other. Also, the retention times of the earliest four analytes (i.e., fluoride, acetate, formate, and chloride) were shifted much later. This phenomenon occurred on all AG11/AS11/TAC-LP1 column sets tried, and even when up to eight rinse vials were used. An in-depth search of the cause was beyond the scope of this project; however, the spiking study was completed on the AS11 to see how the data behaved statistically.

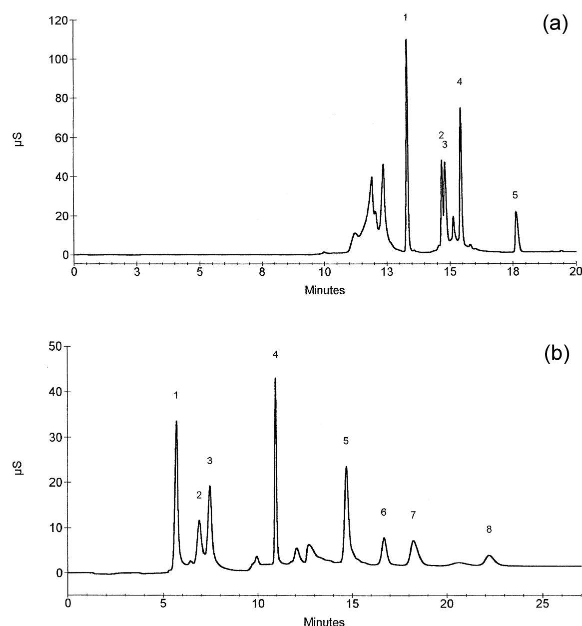

Fig. 2. Example chromatograms of 30-ppb peroxide-based standards on: (a) the AS11 column and (b) the AS15 column. Peak identities on the AS11: (1) chloride, (2) bromide, (3) nitrate, (4) sulfate, and (5) phosphate. Peak identities on the AS15: (1) fluoride, (2) acetate, (3) formate, (4) chloride, (5) sulfate, (6) bromide, (7) nitrate, and (8) phosphate. Plots are from Day 1 of the spiking study.

For the water-based standards on the AS11, the resolution of fluoride and acetate worsened as the spiking study progressed. Therefore, no attempt was made to quantify these two analytes.

On both columns and for both matrices, the retention times of all peaks gradually moved in as the spiking study continued. A possible cause of this R.T. phenomenon would be peroxide degradation of the separator resins. However, checks of levels in the autosampler waste (post-rinsing) showed levels to be less than 0.01%; similar results were obtained on digested peroxides that were checked before the spiking study began. Previous research [5] indicated that these residual-peroxide concentrations should not be detrimental to columns, at least in the short term. Another possibility was that a contaminant in the peroxide concentrated on and then was eluted from the TAC-LP1; subsequently, this species adhered permanently to the separator resins, thereby decreasing capacity. However, no reports of any harmful contaminants in peroxide were found in the literature. It was beyond the scope of this project to find the solution to this behavior. Instead, the spiking study was completed in its entirety to see how the data behaved statistically.

3.2.2.3. Statistical evaluation of retention-time stabilities

The retention-time statistics discussed in Section 3.1 were calculated for both sets of spiking-study standards; results are given in Tables 3 and 4. When compared with the initial calibrations, the spiking-study average daily ranges and average RSDs were acceptable for the peroxide-based standards on the AS11 and for both types of standards on the AS15. On the AS11, these statistics for the water-based solutions were higher during the spiking study, making peak identification more difficult.

During the spiking study, the shift in the average daily retention times was around three min, except for the peroxides on the AS11; this last set shifted only −0.49 min. Since the average daily ranges were acceptable (excluding water-based standards on the AS11), these large shift values would be of concern

only if the PA statistics were found to be poor in the following analysis (Section 3.2.2.4).

3.2.2.4. Statistical analysis of peak-area data

As with the initial-calibration results, the PA data first were inspected for trends. Again, no practically important trends were seen.

Next, mean absolute deviations were calculated as outlined in Section 3.2.2.1. To provide a yardstick for comparison, M.A.D.s were determined for the initial-calibration solutions, as well as for the two sets of standards in the spiking study. All numbers are reported in Table 5. For this research, mean absolute deviations of 3 ppb or lower were considered acceptable for all inorganic ions, and 10 ppb or lower for the two organic acids; values that exceeded this limit are given in bold type in the table.

On both columns, all initial overall M.A.D.s were less than one ppb. These values, then, were the best that could reasonably be expected in future work, and were well below the acceptable levels. For the spiking studies, all M.A.D.s were acceptable, except for acetate and formate on the AS15 (in three of four cases). These occurrences most likely were due to contamination during handling. These results were achieved despite the retention-time instability discussed in Section 3.2.2.3.

(Strictly speaking, M.A.D. is not the best estimate of variability for curves requiring weighted least squares (WLS) (here, fluoride, formate, and sulfate on the AS11, and nitrate on the AS15); since the standard deviation is not constant in these cases, mean relative deviation (M.R.D.) possibly would be more appropriate. However, the latter calculation assumes *relative* standard deviation is constant. In the WLS cases in this research, M.R.D. results indicated that RSDs varied widely, thereby giving misleading summary statistics. At the same time, absolute deviations were quite stable throughout; therefore, M.A.D. values were used for the WLS cases.)

3.2.2.5. Follow-up studies

Following the conclusion of the spiking study, a brief investigation was conducted into the cause of the retention-time reduction. Since the AS15 was the more promising of the two columns, that system was chosen for the investigation. A new AG15 and AS15 were installed, equilibrated, and challenged with a 30-ppb standard in DI water. The retention times of all analytes immediately returned to the values expected for a new AG/AS15 set, indicating that the old resins had indeed been altered. New eluent was then prepared and the new columns were allowed to equilibrate thoroughly. Next, sets of injections were chromatographed in the following order: (1) 11

Table 5
Mean absolute deviations (M.A.D.s) for the overall studies[a]

Column	M.A.D. (ppb)							
	Fluoride	Acetate	Formate	Chloride	Bromide	Nitrate	Sulfate	Phosphate
Initial calibration								
AS11	0.13	0.42	0.75	0.22	0.15	0.30	0.29	0.14
AS15	0.22	0.60	0.66	0.26	0.37	0.38	0.57	0.53
Spiking study: peroxide-based standards								
AS11				0.37	2.73	1.73	1.45	0.86
AS15	2.92	**11.47**	**27.83**	1.16	1.87	1.34	1.77	1.38
Spiking study: water-based standards[b]								
AS11			1.05	0.48	0.38	0.52	0.68	0.88
AS15	0.90	1.74	**20.14**	0.96	1.82	1.45	0.56	2.13

[a] See Sections 3.2.2.1 and 3.2.2.4 for details on calculations. M.A.D.s above 3.0 ppb (10 ppb for acetate and formate) are given in bold type. For each day, M.A.D.s for the common anions were all below 3.0 ppb except for the following peroxide-based standards: (1) bromide twice (3.69 and 3.07 ppb) on AS11; (2) nitrate once (4.17 ppb) on AS11; (3) fluoride twice (4.21 and 7.40 ppb) on AS15; and sulfate once (3.04 ppb) on AS15.

[b] Date from day 7 not included for either column because of autosampler failure on the AS11 system.

replicates of a 30-ppb standard in DI water, (2) 11 replicates of a 30-ppb standard in 30% H_2O_2, and (3) 11 replicates of the same standard as in (1).

To assess the effect of the peroxide injections on the column, the mean retention times of the five latest peaks (chloride, sulfate, bromide, nitrate, and phosphate) were calculated for each group of water-based solutions (i.e., sets 1 and 3 above). All averages in set 3 had decreased, relative to set 1. The differences were 0.04, 0.09, 0.15, 0.20, and 0.34 min, respectively; all differences were roughly twice the standard deviation of their respective retention-time means.

These data indicated that the peroxide-based standards began altering the resins significantly, as soon as these analyses were undertaken. Such attack was occurring even though the peroxide level going onto the AS15 was less than 0.01% (as discussed in Section 3.2.2.2).

4. Conclusions

Coupled with the matrix-elimination procedure outlined above, neither the AS11 nor the AS15 column (2-mm format) provides ideal chromatography of anions in 30% hydrogen peroxide. Retention times gradually shorten as the number of H_2O_2 samples increases.

However, for each concentration tested, statistical analyses generally revealed acceptable stability of the peak areas over time (the exceptions were acetate and formate on the AS15; both analytes were prone to contamination during the spiking study). In addition, when the initial calibration curves were used to predict concentrations for all spiking-study solutions, the overall M.A.D.s were below the quality objective of $\leq$ 3 ppb on both columns for all common anions.

While acceptable results could be obtained using the AS11 column, this separator exhibited several problems during the spiking studies, thereby preventing recommendation of this column. First, retention times did not correspond well between equivalent water-based and peroxide-based standards. Second, the front end (fluoride, acetate, and formate) of the peroxide chromatograms were not resolved sufficiently for quantitation purposes. Third, the average daily range (and average RSD) of the retention time was quite high for the test anion, Cl^-, in water. Fourth, bromide and nitrate were not completely resolved from each other, making identification difficult if only one species was present; in addition, quantitation was questionable if widely varying levels of the two anions existed in a given solution.

On the other hand, this research shows that this matrix-elimination approach could be used to analyze peroxide samples on the microbore AS15. When testing samples, the AS15 protocol should be as follows. First, conduct a thorough calibration study, using water-based standards. Include sufficient concentrations in the critical areas of the range. Analyze all data statistically to develop appropriate calibration curves for use with samples. Second, analyze samples. Third, if there was a positive background for any analyte in the initial-calibration standards, subtract the blank's mean PA from the corresponding sample PA before predicting concentrations. This step is taken because the background contamination found in the calibration blank will not be present in the samples, and should not be included in quantifying samples. Fourth, predict the concentrations, using the above calibration curves. Fifth, correct for the density (1.11) of peroxide. Sixth, include check standards. Monitor the calibration curves' performances using one (or more) water-based standard. If necessary, confirm peak identities and predicted concentrations, using a mid-range spiked peroxide and a peroxide-based blank.

From a cost standpoint, using the above approach with the AS15 will be higher than typical for two reasons. First, a heated enclosure is required. However, that expense is outweighed by the improved reliability of the chromatography (compared to the AS11). Second, the matrix will age the resins prematurely. Nevertheless, the columns used here were still viable at the end of the research, even after being subjected to over 100 peroxide samples.

Lastly, two precautions should be observed when handling samples and standards. First, extreme care should be taken to eliminate contamination sources of acetate and formate, since these analytes were found to be difficult to control. Second, autosampler vials of peroxide should be monitored. Occasionally, bubbles formed inside the container. While this condition never affected peak areas adversely, the bubbles could push a drop of liquid out of the vial. If

this bead were to come in contact with the sensor in the autosampler, the AS40 might read subsequent vials as rinse vials.

In summary, this method has the advantage of being automated and free of sample-pretreatment steps. Even though not all classical criteria are met when using the above AS15 protocol, the procedure has been shown to be feasible and statistically sound. Thus, the primary objective of any method has been met: generation of reliable quantitative results that meet quality objectives.

5. Nomenclature

5.1. Mathematical symbols used

α nominal probability of false positives.
β nominal probability of false negatives.
R^2_{adj} a version of R^2, ''penalized'' for each independent variable used in the regression. (R^2 measures the amount of total variation in the response ''explained'' by the dependent variable.)

5.2. Terms and abbreviations used

Average daily range average of the daily retention-time ranges, where range is ''maximum daily R.T. minus minimum daily R.T.''.
Average RSD average RSD for the average daily retention time.
DL detection limit. The concentration below which the analytical method cannot reliably detect a response.
M.A.D. mean absolute deviation. The mean of the absolute value of the quantity ''true minus predicted''.
M.R.D. mean relative deviation. The mean of the absolute value of the quantity ''(true minus predicted) divided by true'', expressed as a percentage.
OLS ordinary least squares. A fitting technique that minimizes the sum of squares of the residuals.
p.i. prediction interval. A pair of limits that bracket the uncertainty in one future measurement.
RSD relative standard deviation. The sample standard deviation divided by the sample mean, expressed as a percentage.
R.T. retention time, in min.
Shift shift in the average daily retention time over the course of the study, where the difference is ''final minus initial''.
WLS weighted least squares. Same methodology as OLS, except weights are incorporated to account for non-constant response variation.

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