US 20090078862A1

(19) **United States**

(12) **Patent Application Publication**

RODIER et al.

(10) **Pub. No.: US 2009/0078862 A1**

(43) **Pub. Date: Mar. 26, 2009**

(54) **ION MOBILITY SPECTROMETRY ANALYZER FOR DETECTING PEROXIDES**

(76) Inventors: **Dan RODIER**, Louisville, CO (US); **Allan T. Bacon, JR.**, Parkton, MD (US)

Correspondence Address:
GREENLEE WINNER AND SULLIVAN P C
4875 PEARL EAST CIRCLE, SUITE 200
BOULDER, CO 80301 (US)

(21) Appl. No.: **12/182,343**

(22) Filed: **Jul. 30, 2008**

Related U.S. Application Data

(60) Provisional application No. 60/952,669, filed on Jul. 30, 2007, provisional application No. 60/953,879, filed on Aug. 3, 2007, provisional application No. 60/984,804, filed on Nov. 2, 2007.

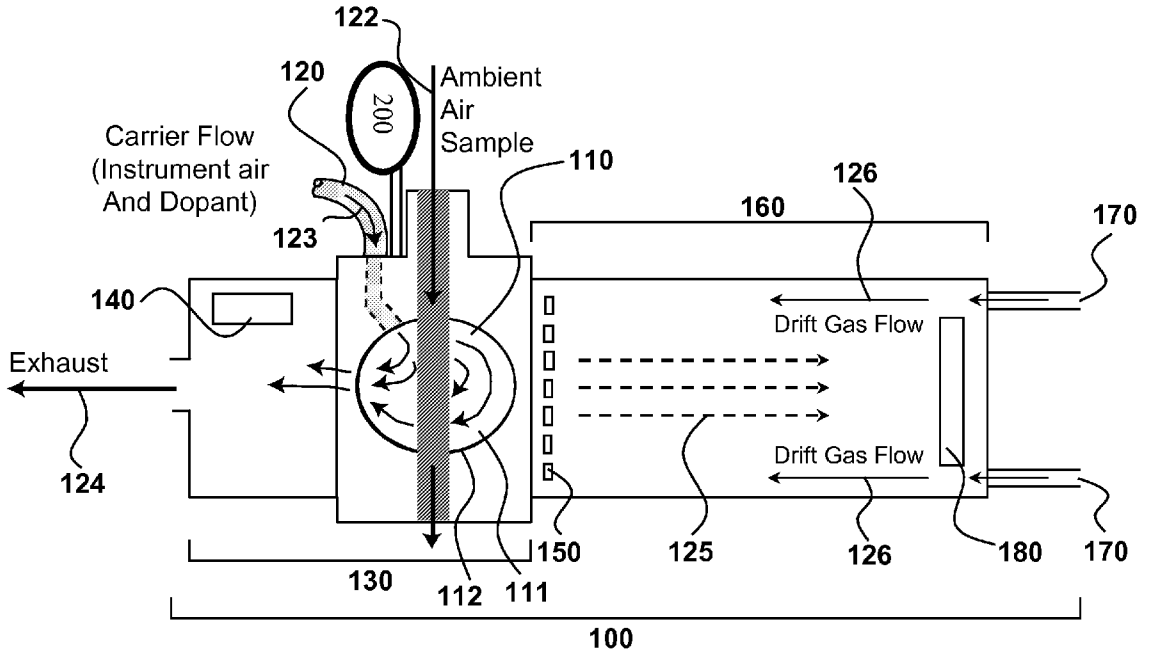
Publication Classification

(51) **Int. Cl.**
B01D 59/44 (2006.01)

(52) **U.S. Cl.** **250/282**; 250/288

(57) **ABSTRACT**

The present invention provides IMS analyzers and methods for detecting, identifying, and characterizing (e.g., measuring the concentration of) peroxides in samples. Methods and systems of the present invention utilize sample inlet conditions and dopant strategies providing an enhancement in selectivity and sensitivity for the detection of peroxide compounds relative to conventional IMS analyzers. Dopants of the present invention include, but are not limited to, substituted aryl compounds or substituted cyclic dienes; wherein the substituted aryl compound or the substituted cyclic diene has at least one substituent selected from the group consisting of a hydroxyl group, a carbonyl group, an aldehyde group, an ester group, a carboxylic acid group and a carbonate ester group. The present IMS analyzers and methods are versatile and enable selective detection of a broad class of peroxides and derivatives thereof, including hydrogen peroxide, hydroperoxides, organic peroxides and derivatives thereof.



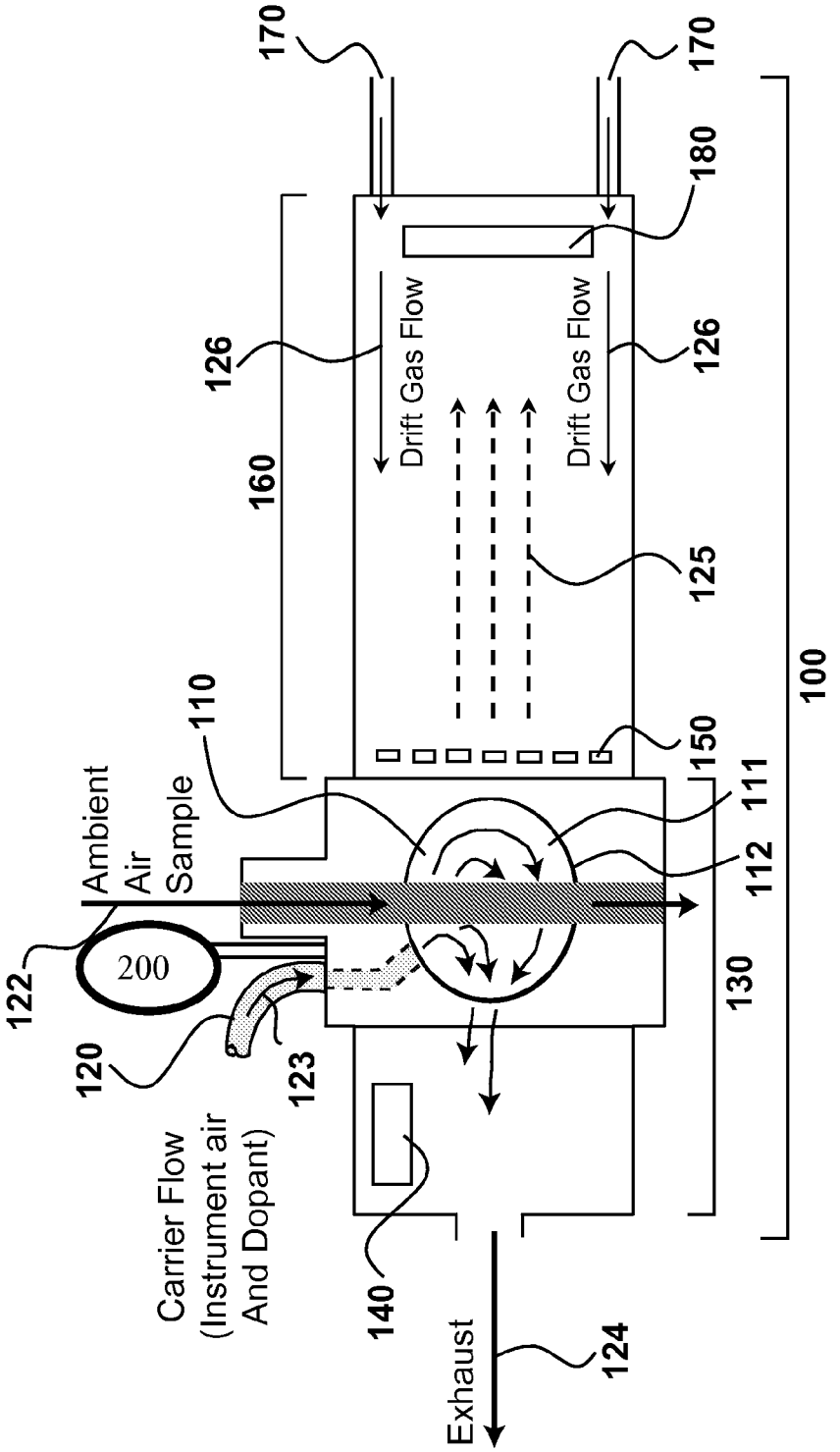

170
170
180
126
126
Drift Gas Flow
Drift Gas Flow
160
125
150
110
111
112
100
Ambient
Air
Sample
122
200
120
123
130
Carrier Flow
(Instrument air
And Dopant)
140
Exhaust
124

Figure 1A

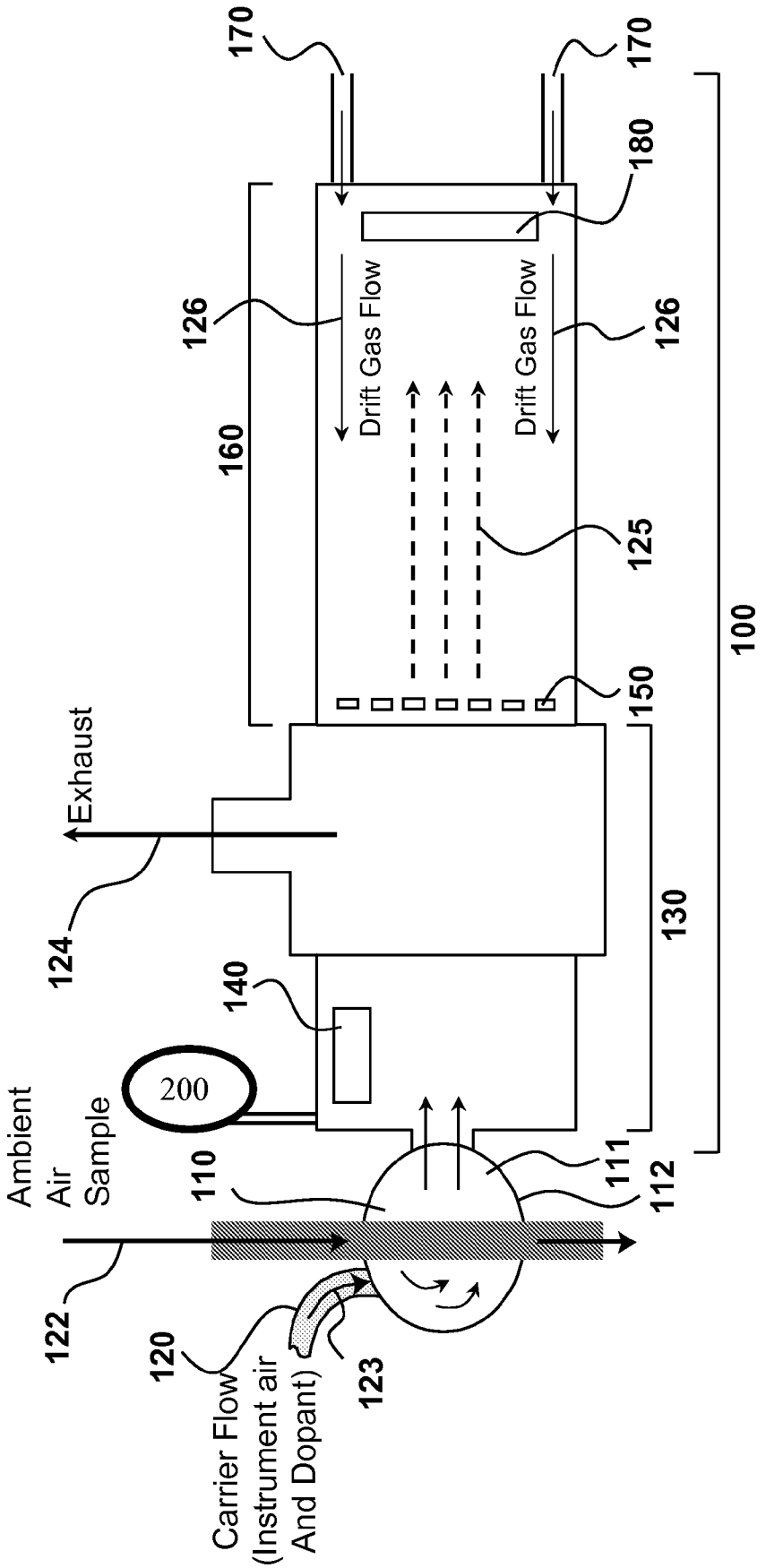

170
170
180
126
126
Drift Gas Flow
Drift Gas Flow
160
125
150
100
Exhaust
124
130
140
200
Ambient
Air
Sample
110
111
112
122
120
123
Carrier Flow
(Instrument air
And Dopant)

Figure 1B

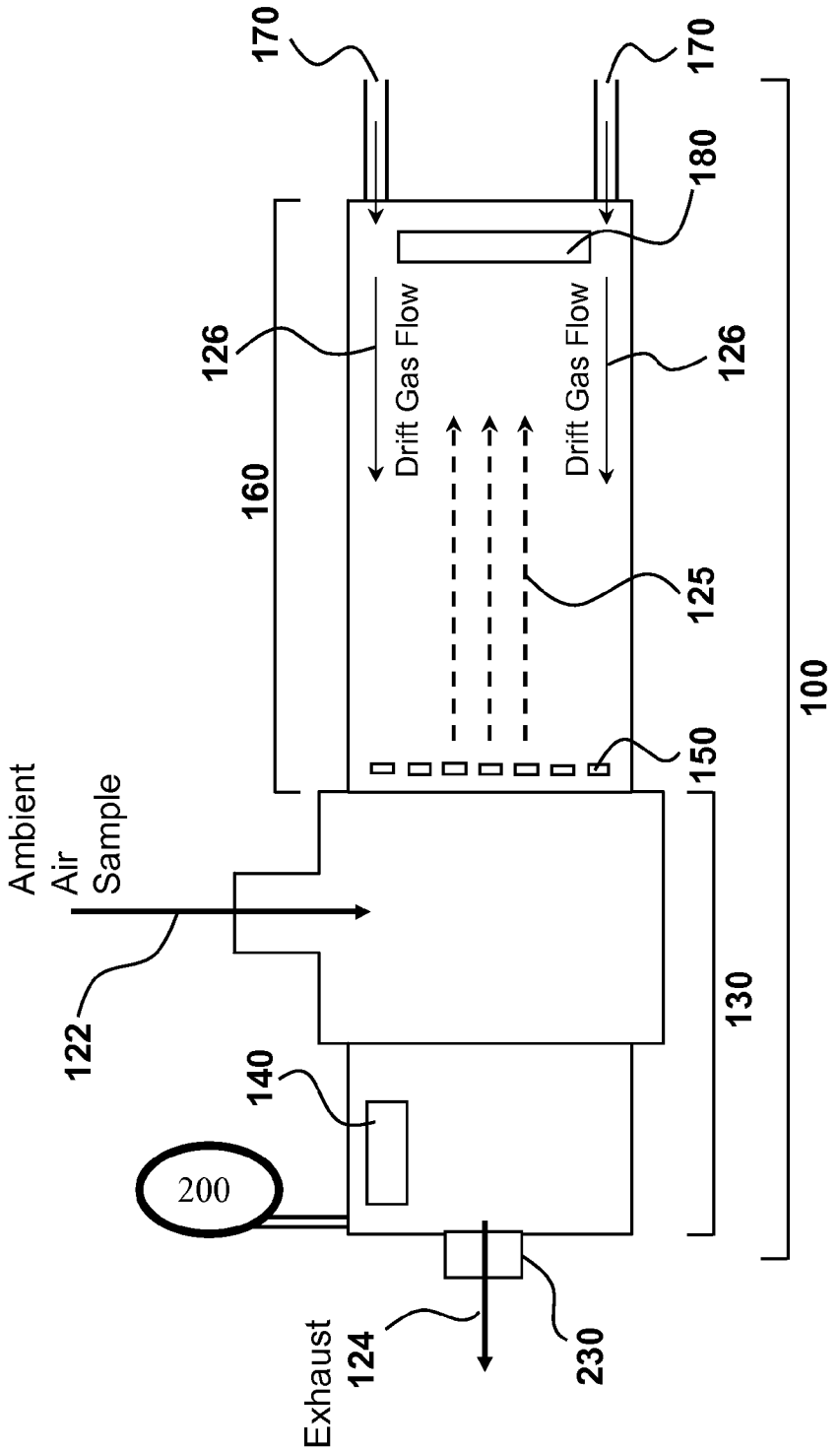

170
170
180
126
126
Drift Gas Flow
Drift Gas Flow
160
125
150
100
Ambient
Air
Sample
122
140
130
200
Exhaust
124
230

Figure 1C

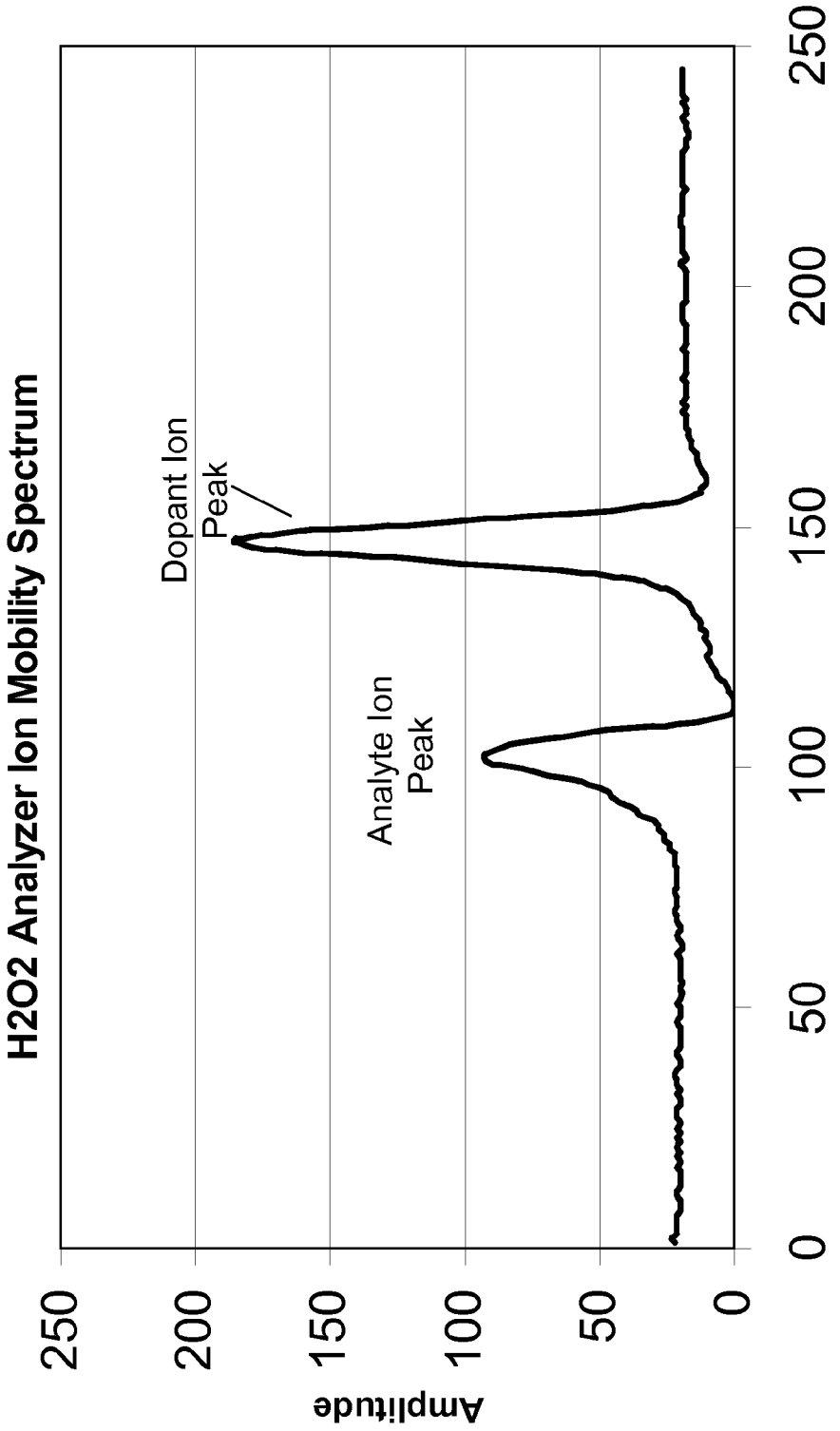

H2O2 Analyzer Ion Mobility Spectrum
Dopant Ion Peak
Analyte Ion Peak
Amplitude
0
50
100
150
200
250
Time bin (1000 +80x)
0
50
100
150
200
250

Figure 2

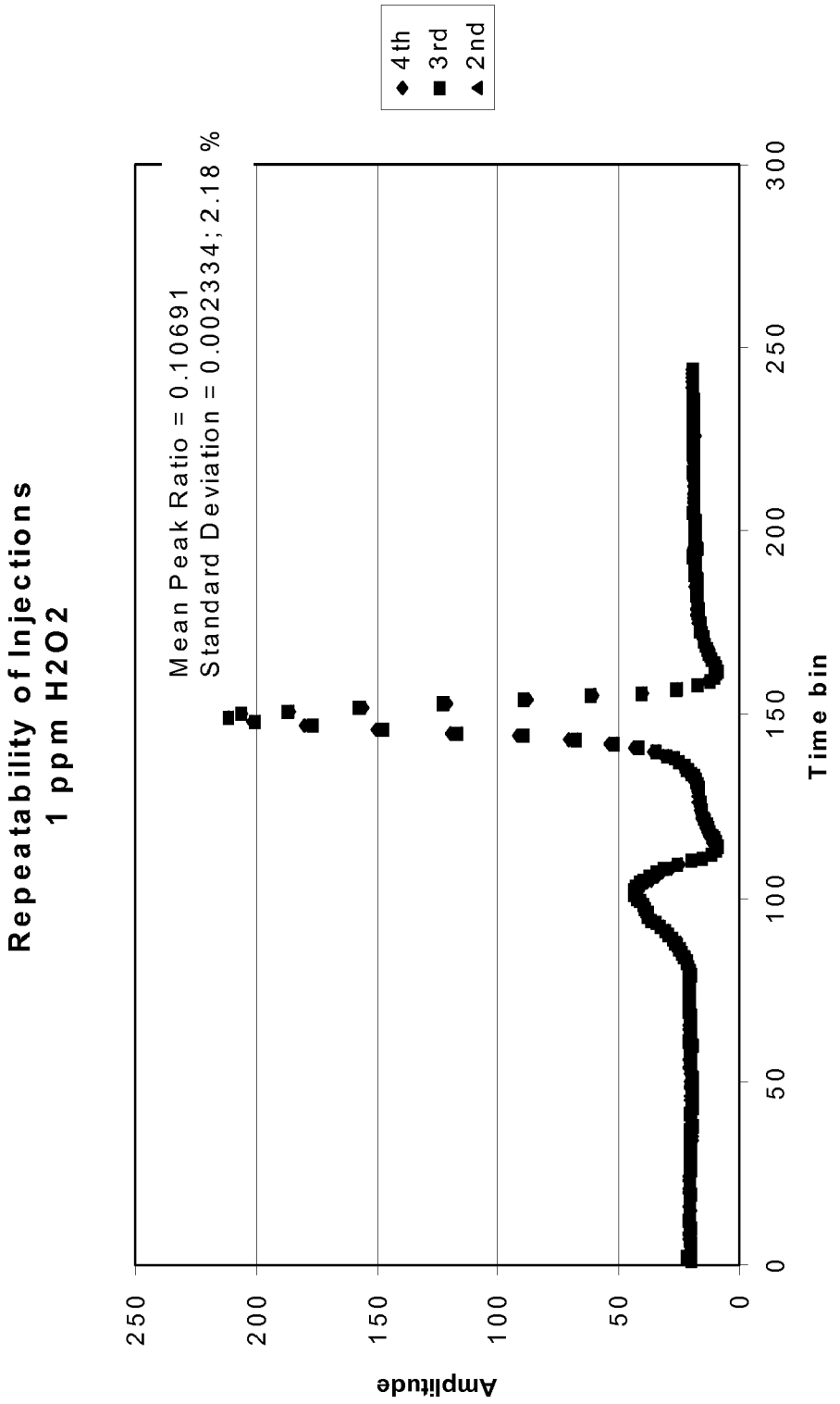

Repeatability of Injections
1 ppm H2O2
Mean Peak Ratio = 0.10691
Standard Deviation = 0.002334; 2.18 %
4th
3rd
2nd
Amplitude
Time bin
0
50
100
150
200
250
300

Figure 3

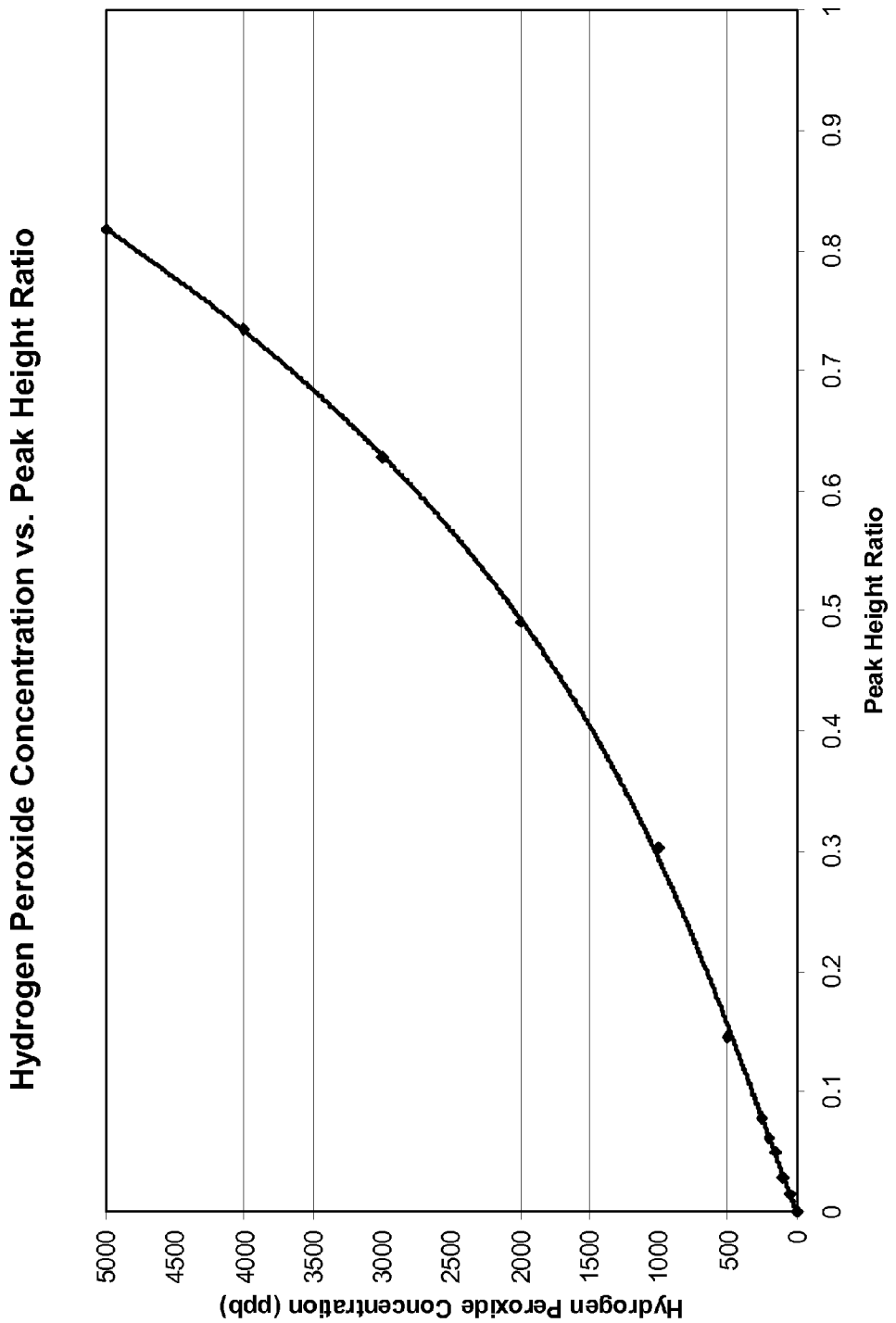

Hydrogen Peroxide Concentration vs. Peak Height Ratio
Hydrogen Peroxide Concentration (ppb)
5000
4500
4000
3500
3000
2500
2000
1500
1000
500
0
0
0.1
0.2
0.3
0.4
0.5
0.6
0.7
0.8
0.9
1
Peak Height Ratio

Figure 4

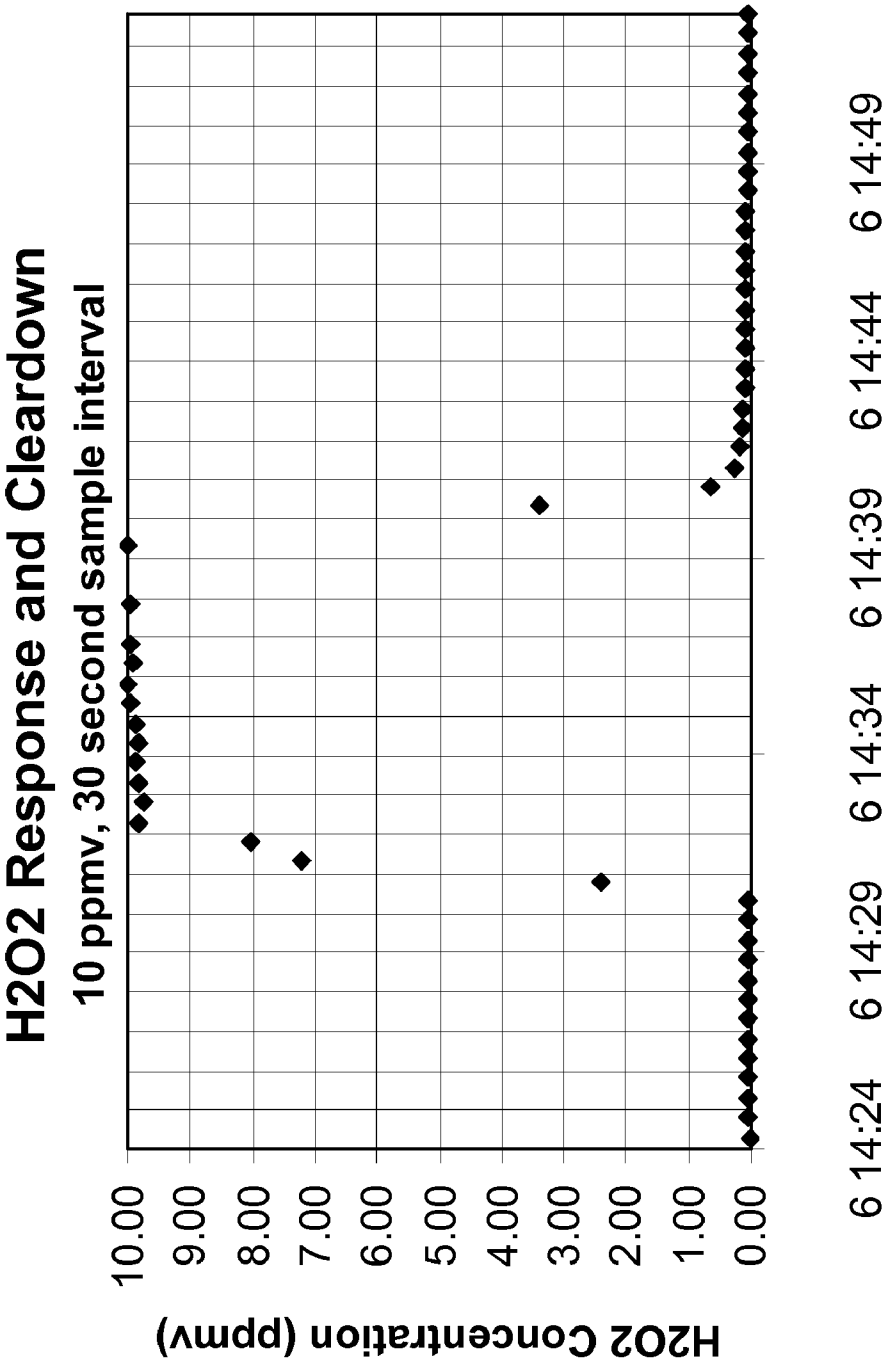

H2O2 Response and Cleardown
10 ppmv, 30 second sample interval
H2O2 Concentration (ppmv)
10.00
9.00
8.00
7.00
6.00
5.00
4.00
3.00
2.00
1.00
0.00
6 14:24
6 14:29
6 14:34
6 14:39
6 14:44
6 14:49

Figure 5

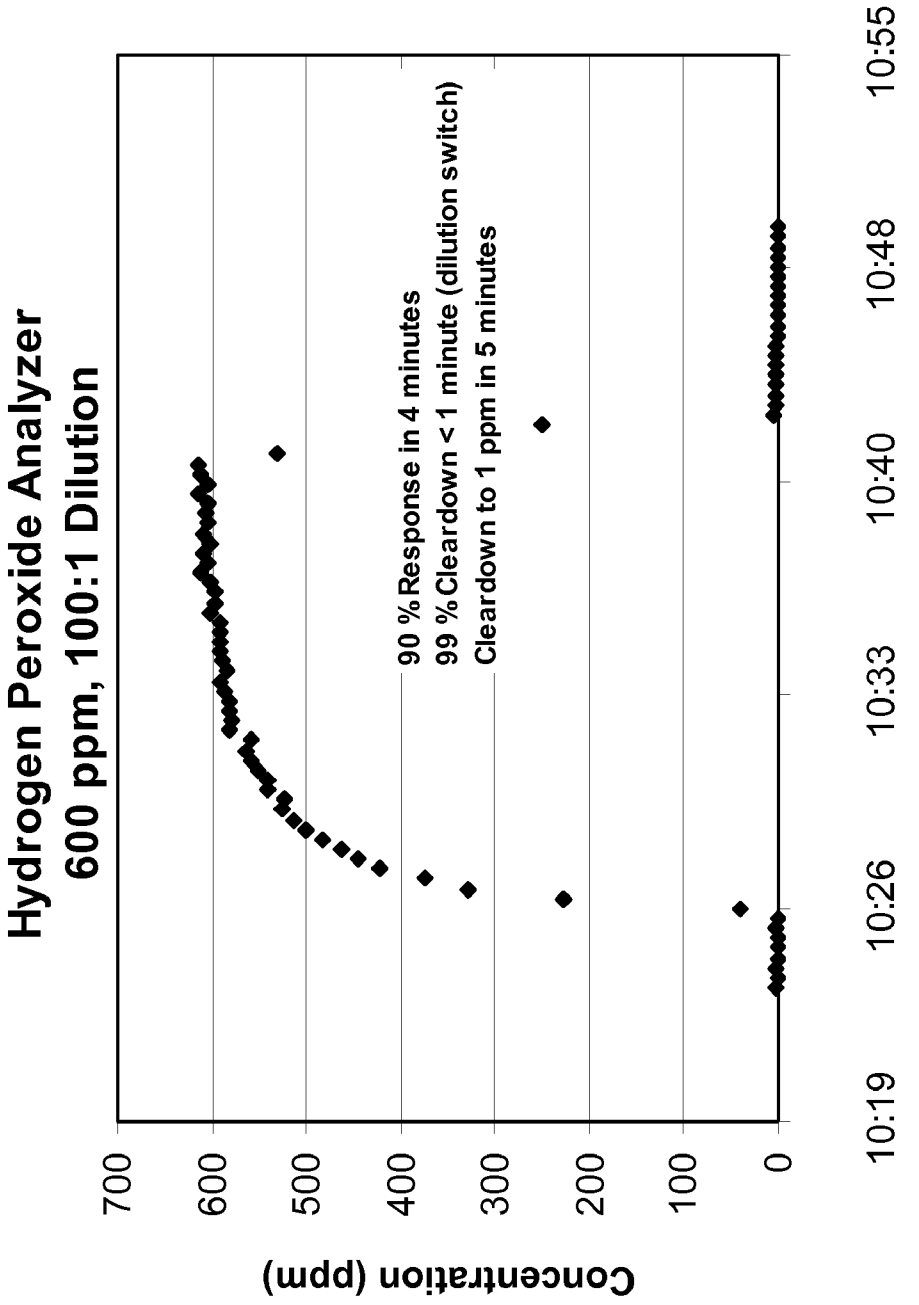

Hydrogen Peroxide Analyzer
600 ppm, 100:1 Dilution
90 % Response in 4 minutes
99 % Cleardown < 1 minute (dilution switch)
Cleardown to 1 ppm in 5 minutes
Concentration (ppm)
700
600
500
400
300
200
100
0
10:19
10:26
10:33
10:40
10:48
10:55

Figure 6

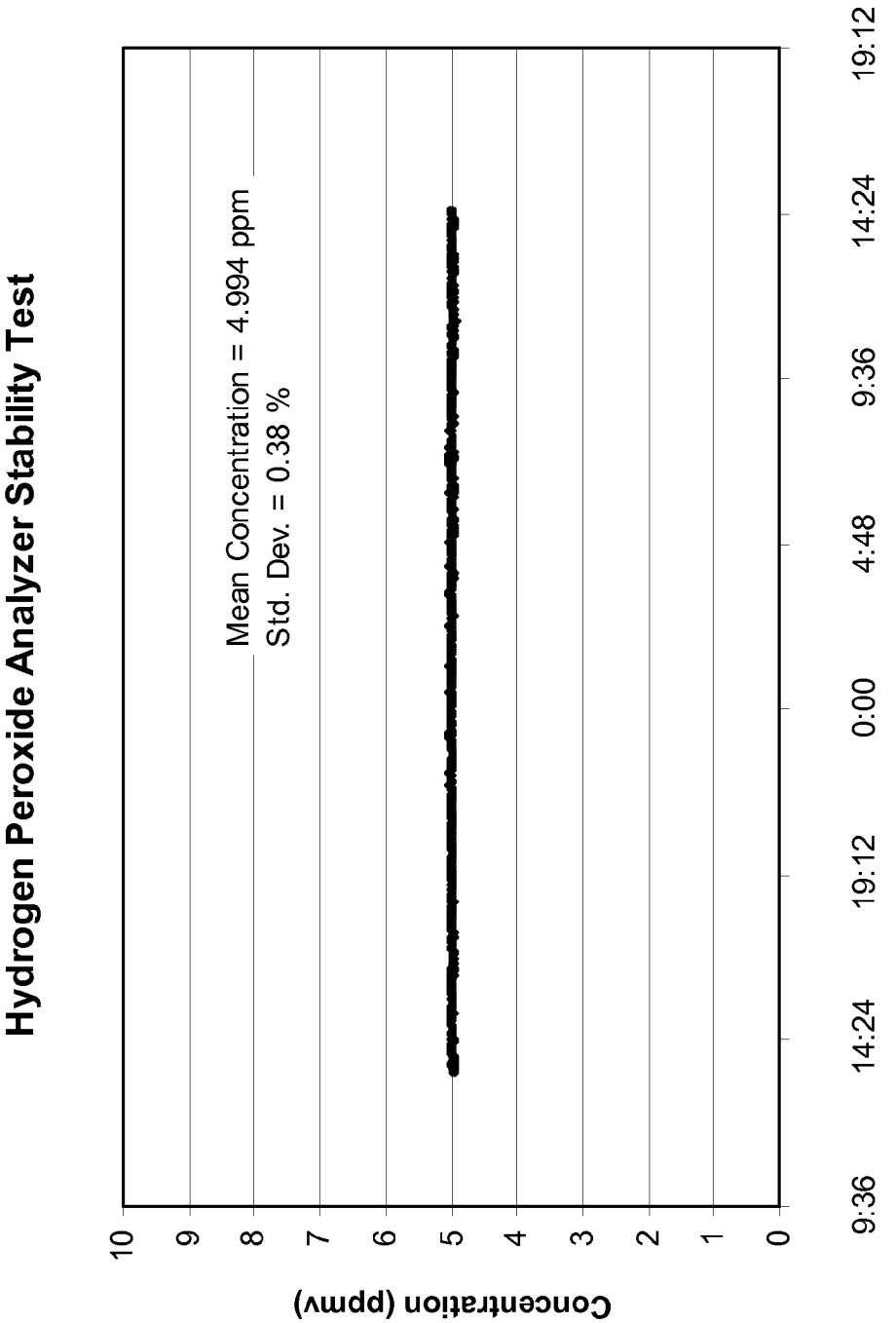

Hydrogen Peroxide Analyzer Stability Test
Mean Concentration = 4.994 ppm
Std. Dev. = 0.38 %
Concentration (ppmv)
10
9
8
7
6
5
4
3
2
1
0
9:36
14:24
19:12
0:00
4:48
9:36
14:24
19:12

Figure 7

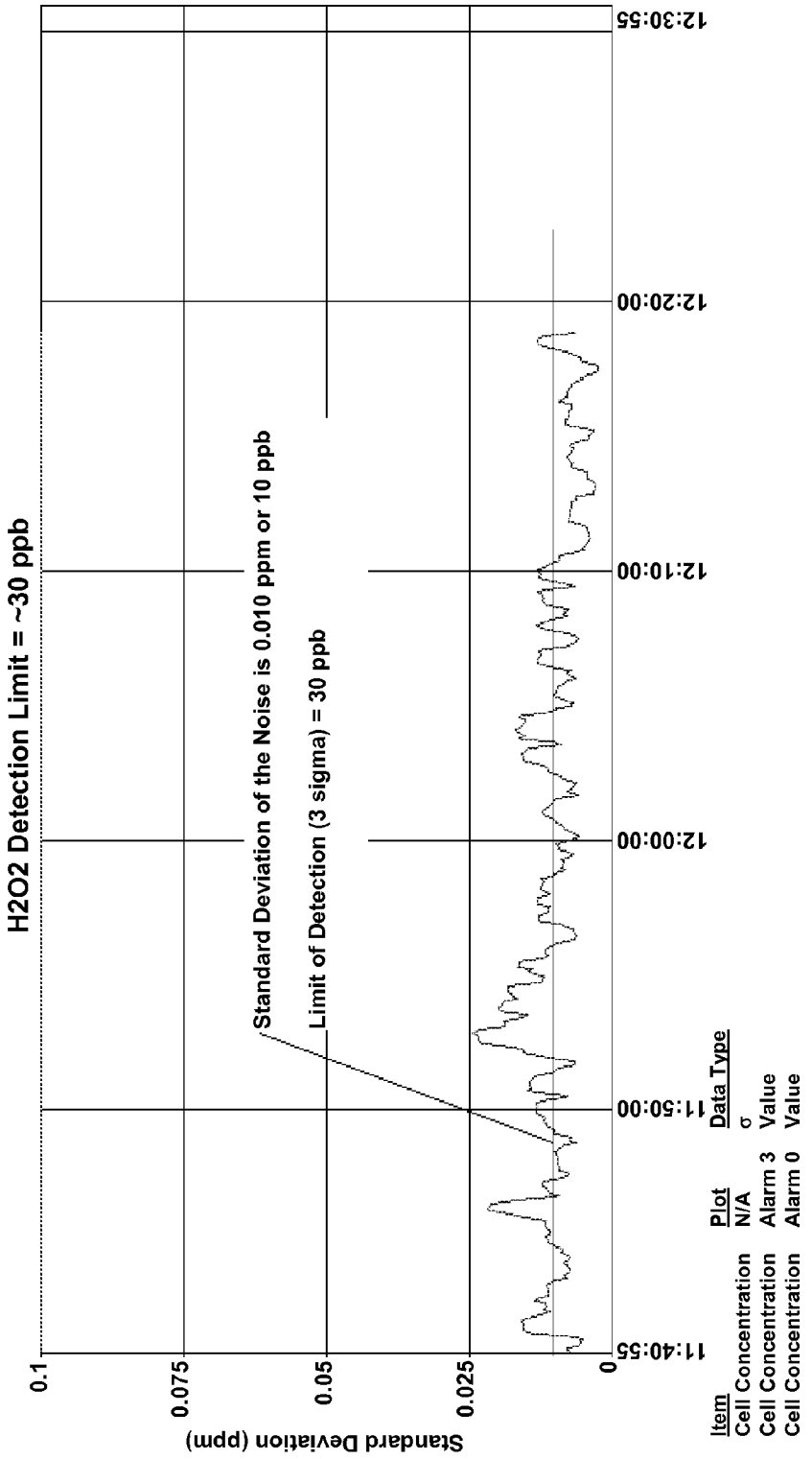

H2O2 Detection Limit = ~30 ppb
Standard Deviation of the Noise is 0.010 ppm or 10 ppb
Limit of Detection (3 sigma) = 30 ppb
Standard Deviation (ppm)
0.1
0.075
0.05
0.025
0
11:40:55
11:50:00
12:00:00
12:10:00
12:20:00
12:30:55
Item Plot Data Type
Cell Concentration N/A σ
Cell Concentration Alarm 3 Value
Cell Concentration Alarm 0 Value

Figure 8

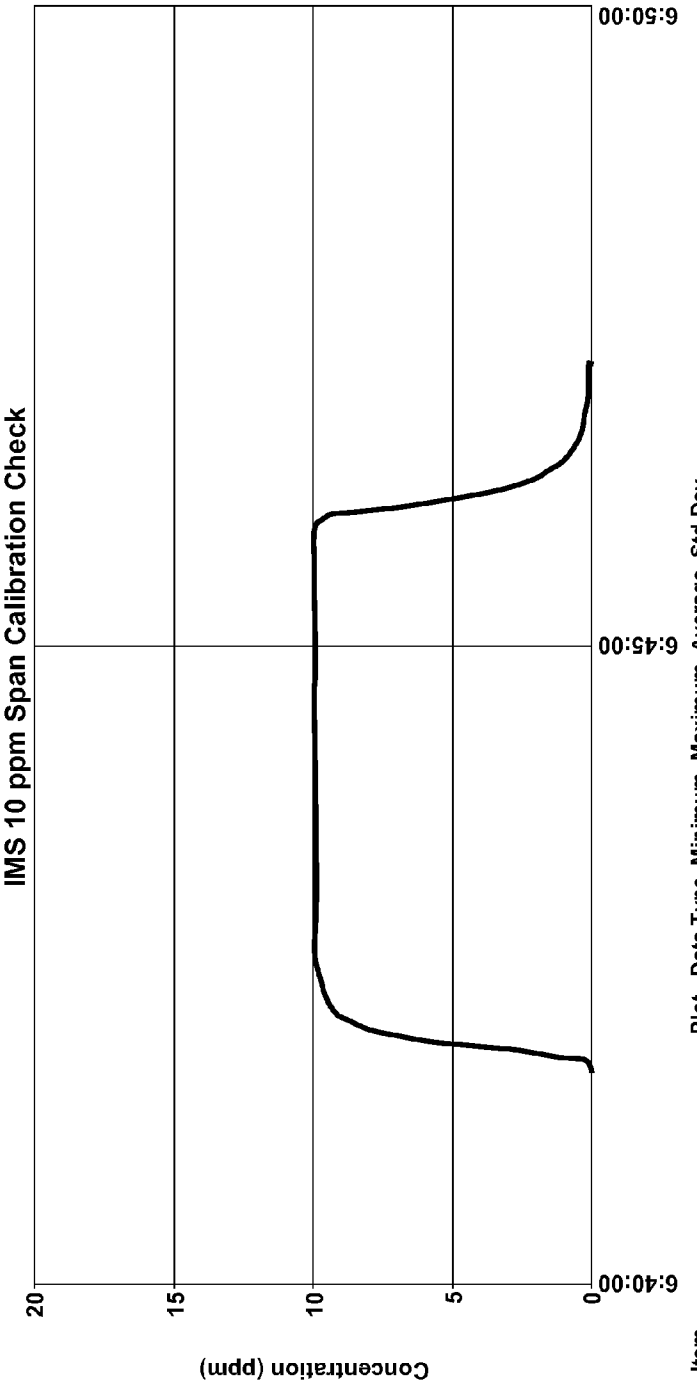

IMS 10 ppm Span Calibration Check
Concentration (ppm)
20
15
10
5
0
6:40:00
6:45:00
6:50:00
Item
High Range Concentration
History Size: 12 samples (Statistics Generated for Plot Duration)
Plot filter: None
Alt. plot filter: None
Filter join: Off
Flyer filter: None
Plot Data Type Minimum Maximum Average Std Dev
PPM Value -0.06 10.07 4.30 4.78

Figure 9

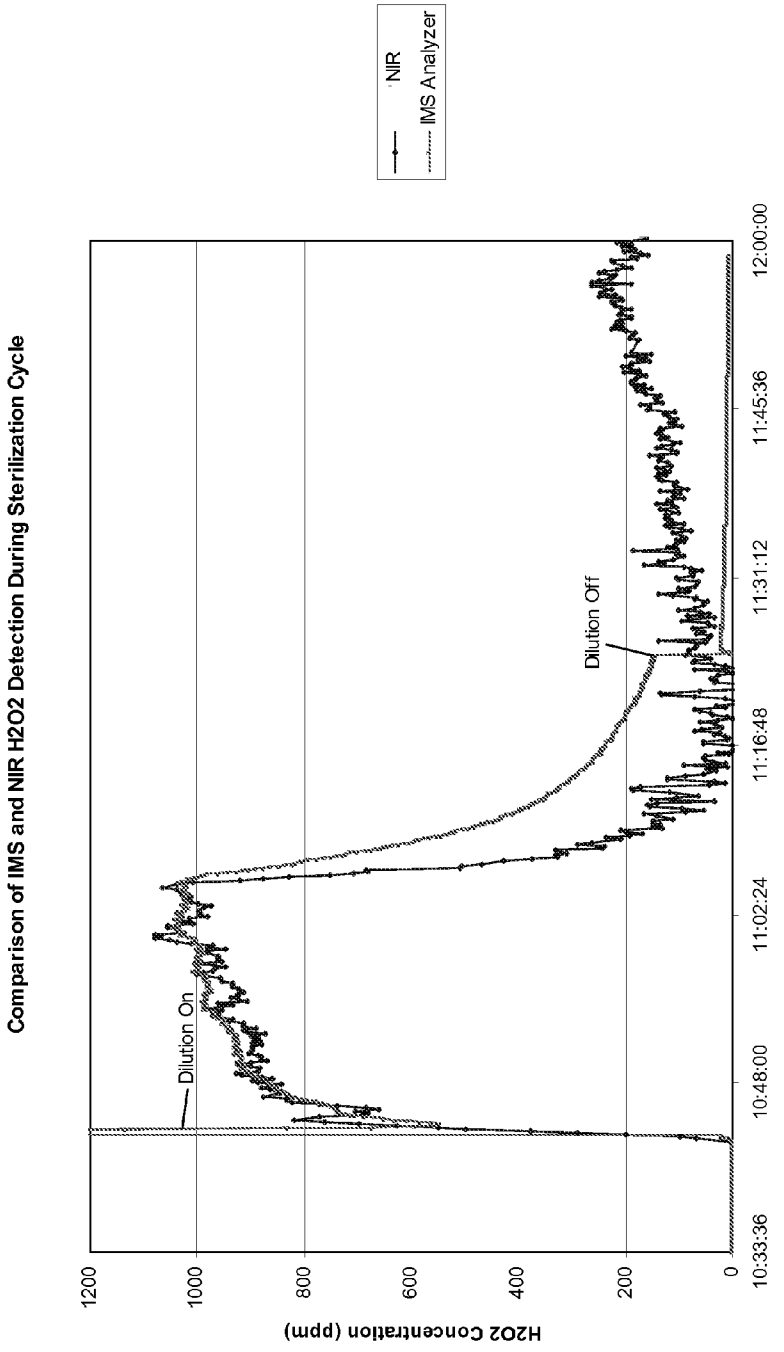

Comparison of IMS and NIR H2O2 Detection During Sterilization Cycle
NIR
IMS Analyzer
H2O2 Concentration (ppm)
1200
1000
800
600
400
200
0
10:33:36
10:48:00
11:02:24
11:16:48
11:31:12
11:45:36
12:00:00
Dilution On
Dilution Off

Figure 10

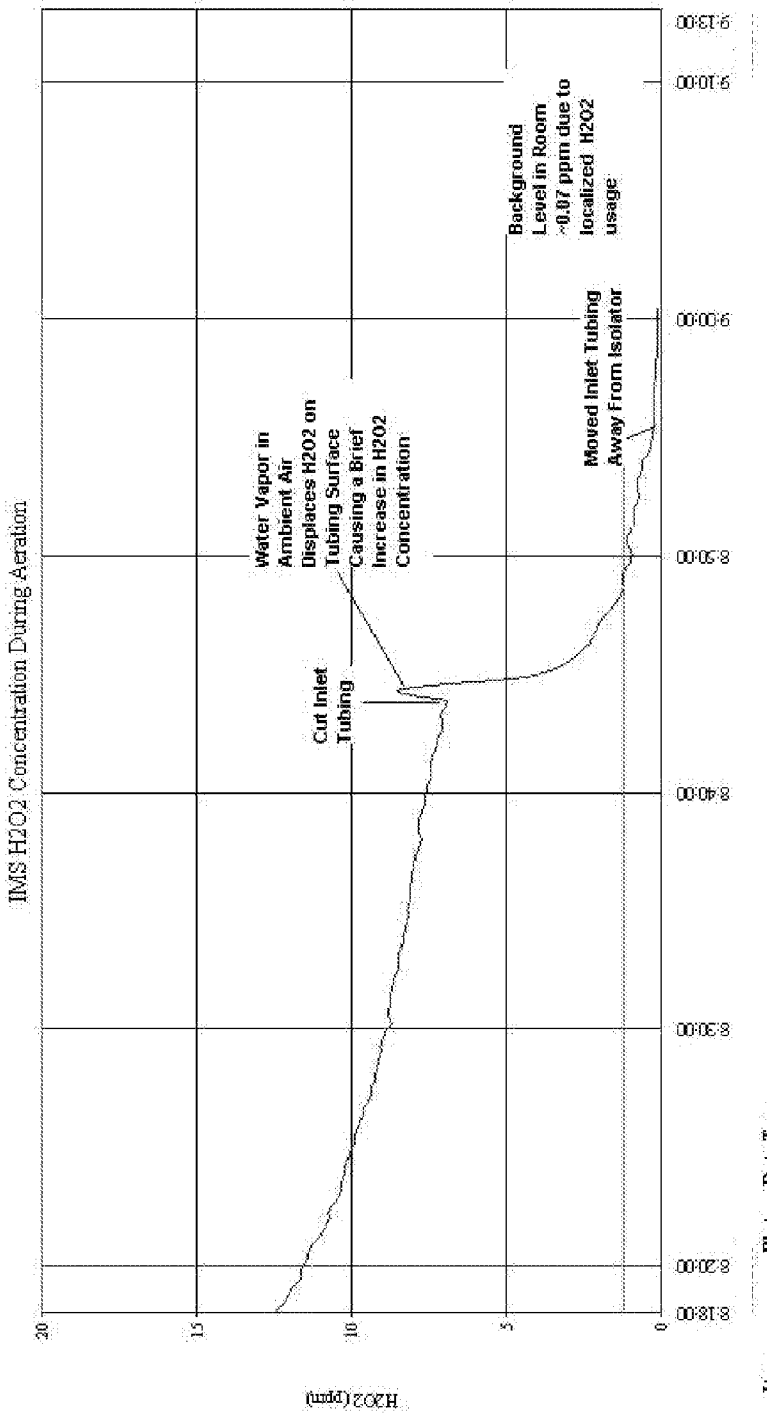

IMS H2O2 Concentration During Aeration
H2O2 (ppm)
20
15
10
5
0
8:10:00
8:20:00
8:30:00
8:40:00
8:50:00
9:00:00
9:10:00
9:13:00
Water Vapor in Ambient Air Displaces H2O2 on Tubing Surface Causing a Brief Increase in H2O2 Concentration
Cut Inlet Tubing
Moved Inlet Tubing Away From Isolator
Background Level in Room ~0.07 ppm due to localized H2O2 usage
Item Plot Data Type
Cell Concentration N/A Avg
Cell Concentration Alarm 3 Value
Cell Concentration Alarm 0 Value
History Size: 6 samples (Statistics Generated For Past 6 Samples)
Plot filter: None
Alt plot filter: None
Filter join: Off
Flyer filter: None

Figure 11

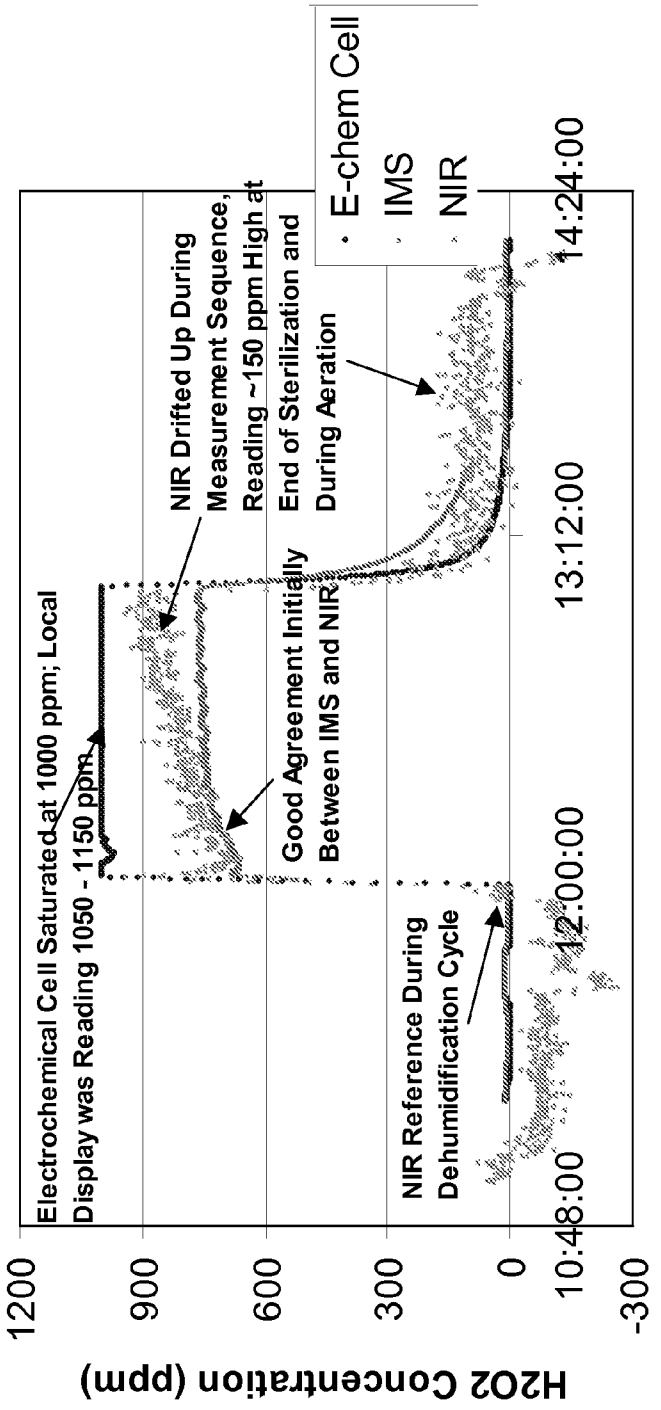

H2O2 Concentration (ppm)
1200
900
600
300
0
-300
10:48:00
12:00:00
13:12:00
14:24:00
E-chem Cell
IMS
NIR
Electrochemical Cell Saturated at 1000 ppm; Local Display was Reading 1050 - 1150 ppm
NIR Drifted Up During Measurement Sequence, Reading ~150 ppm High at End of Sterilization and During Aeration
Good Agreement Initially Between IMS and NIR
NIR Reference During Dehumidification Cycle

Figure 12

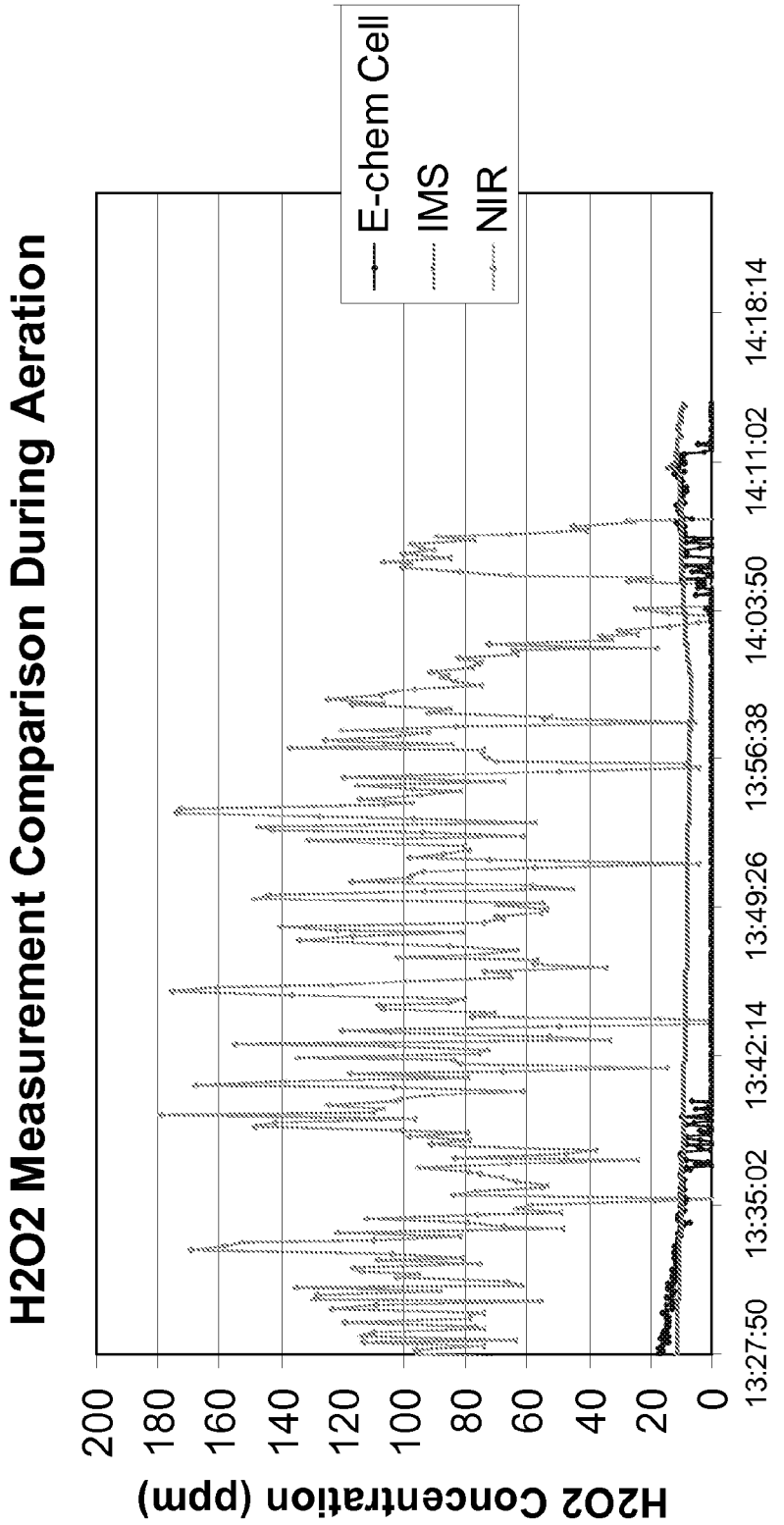

H2O2 Measurement Comparison During Aeration
E-chem Cell
IMS
NIR
H2O2 Concentration (ppm)
200
180
160
140
120
100
80
60
40
20
0
13:27:50
13:35:02
13:42:14
13:49:26
13:56:38
14:03:50
14:11:02
14:18:14

Figure 13

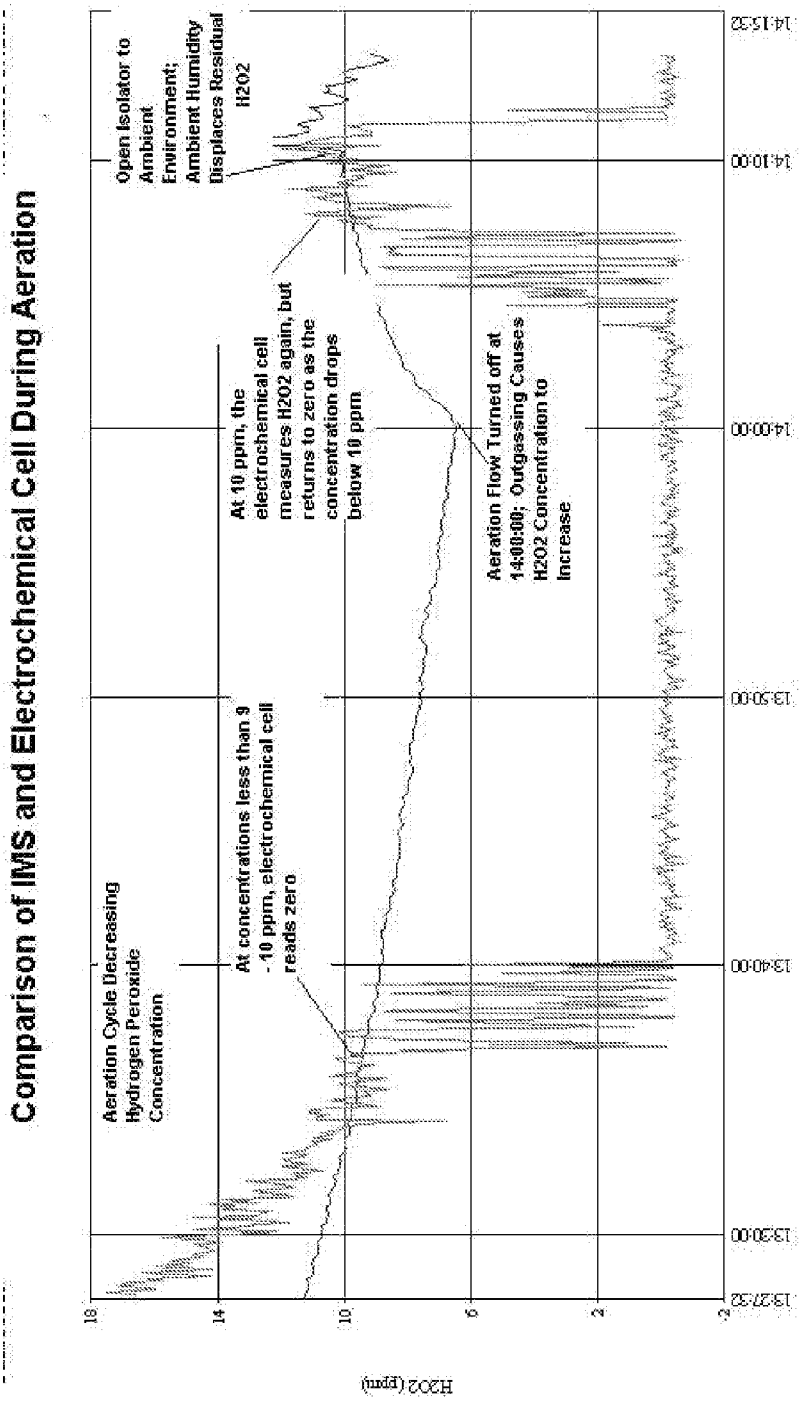

Comparison of IMS and Electrochemical Cell During Aeration
Aeration Cycle Decreasing Hydrogen Peroxide Concentration
At concentrations less than 9 - 10 ppm, electrochemical cell reads zero
At 10 ppm, the electrochemical cell measures H2O2 again, but returns to zero as the concentration drops below 10 ppm
Aeration Flow Turned off at 14:00:00; Outgassing Causes H2O2 Concentration to Increase
Open Isolator to Ambient Environment; Ambient Humidity Displaces Residual H2O2
H2O2 (ppm)
18
14
10
6
2
-2
13:27:32
13:30:00
13:40:00
13:50:00
14:00:00
14:10:00
14:15:32
Item Plot Data Type Minimum Maximum Average Std Dev
Cell Concentration N/A Value 0.99 13.81 7.23 3.29
E-Chem Cell ppm Value -0.74 50.14 9.47 13.39
History Size: 6 samples (Statistics Generated For Plot Duration)
Plot filter: None
Alt plot filter: None
Filter join: Off
Flyer filter: None

Figure 14

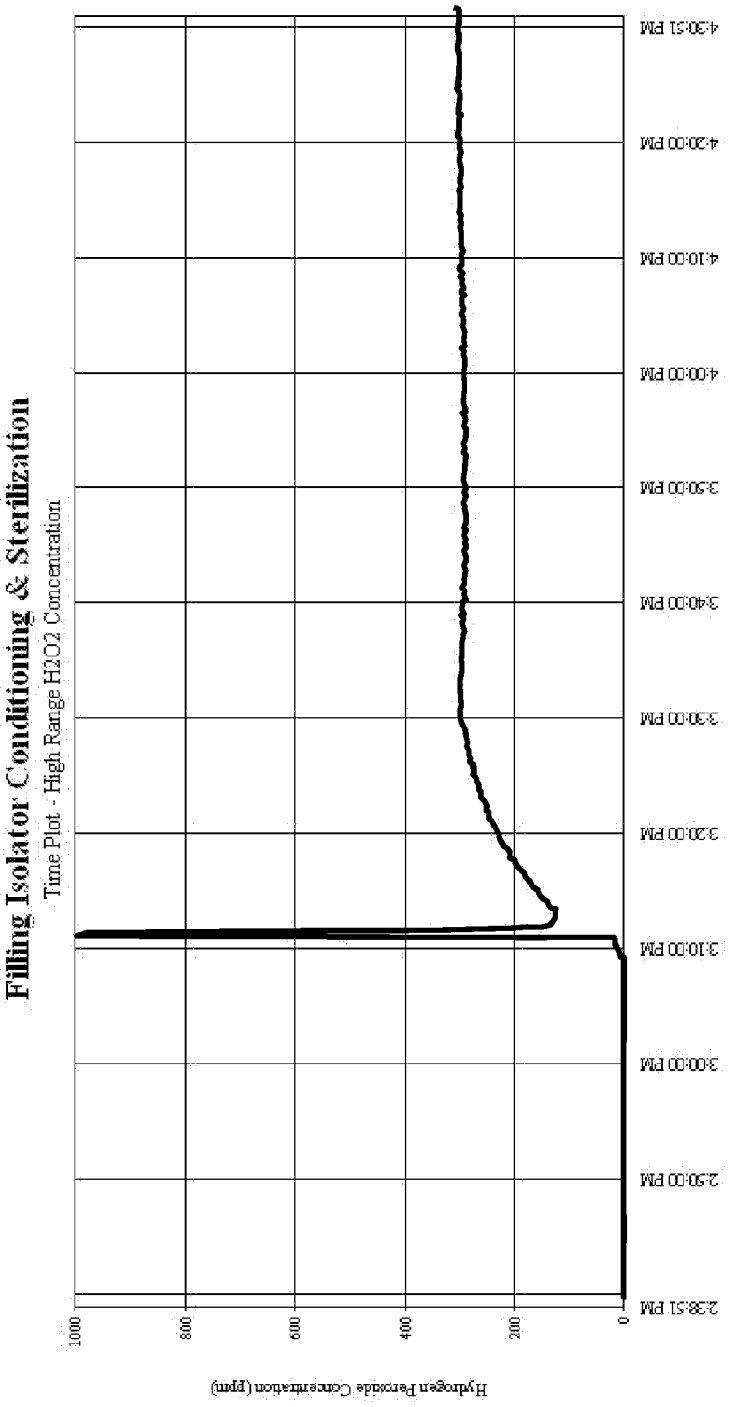

Filling Isolator Conditioning & Sterilization
Time Plot - High Range H2O2 Concentration
Hydrogen Peroxide Concentration (ppm)
1000
800
600
400
200
0
2:38:51 PM
2:50:00 PM
3:00:00 PM
3:10:00 PM
3:20:00 PM
3:30:00 PM
3:40:00 PM
3:50:00 PM
4:00:00 PM
4:10:00 PM
4:20:00 PM
4:30:51 PM

Figure 15

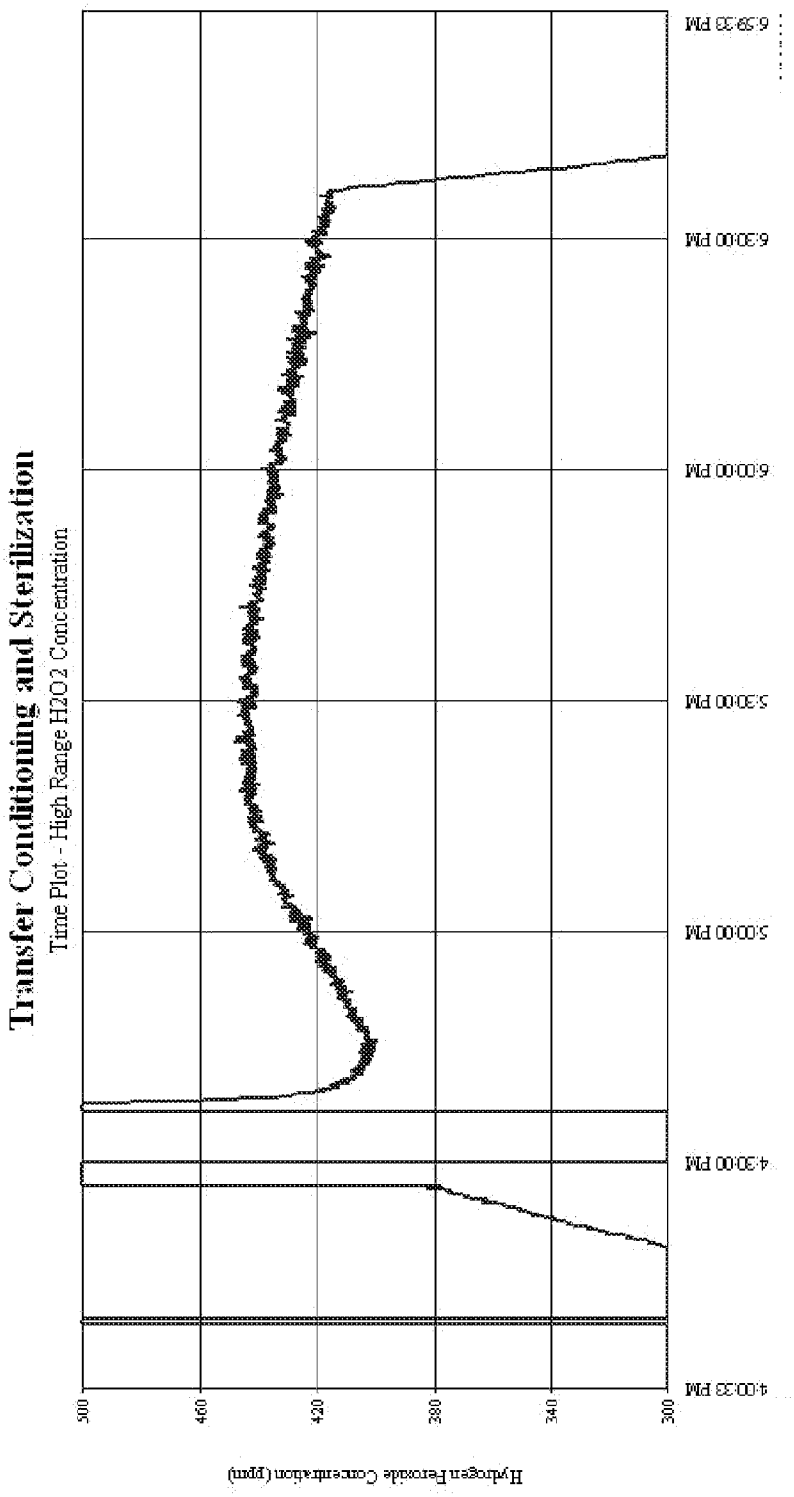

Transfer Conditioning and Sterilization
Time Plot - High Range H2O2 Concentration
Hydrogen Peroxide Concentration (ppm)
500
460
420
380
340
300
4:00:33 PM
4:30:00 PM
5:00:00 PM
5:30:00 PM
6:00:00 PM
6:30:00 PM
6:59:33 PM

Figure 16

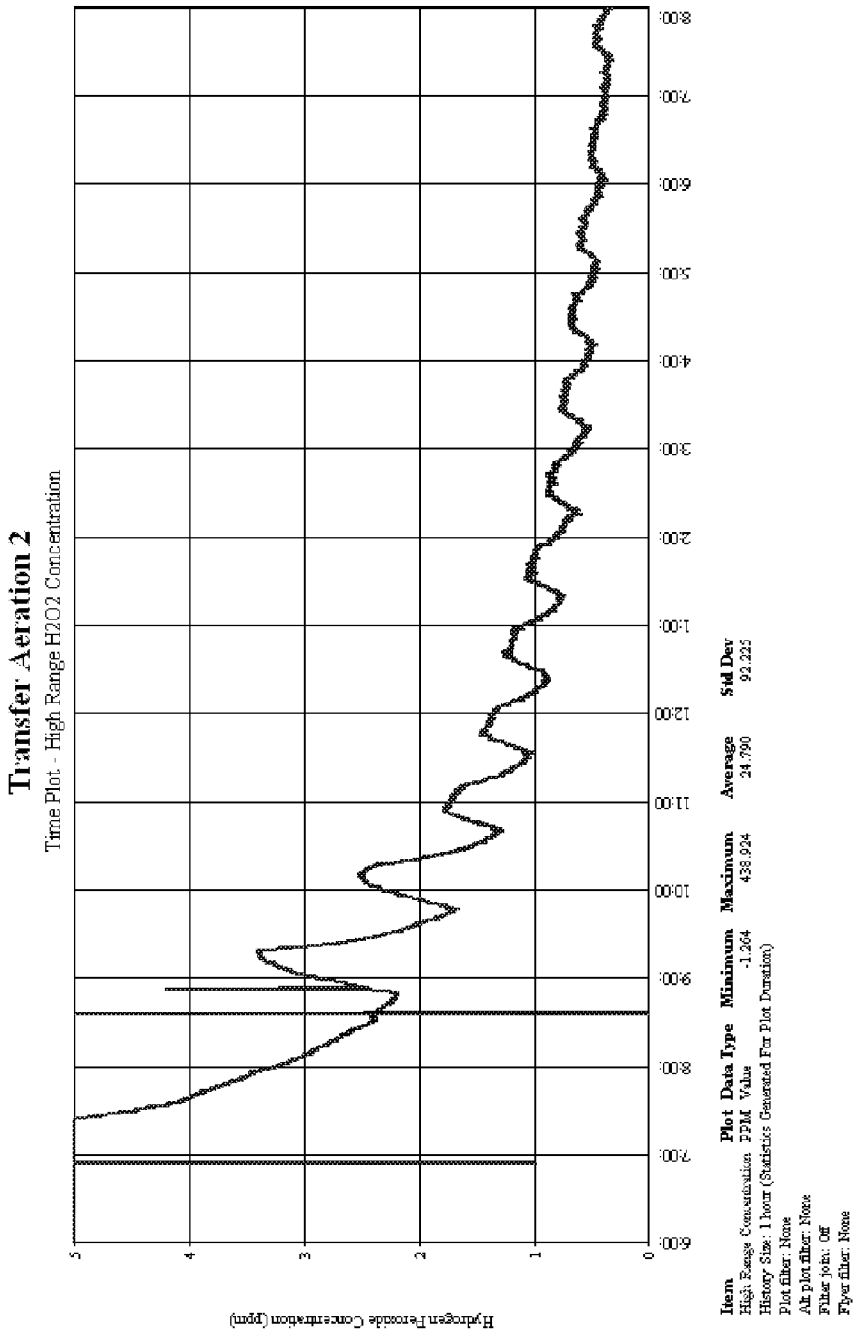

Transfer Aeration 2
Time Plot - High Range H2O2 Concentration
Hydrogen Peroxide Concentration (ppm)
0
1
2
3
4
5
6:00
7:00
8:00
9:00
10:00
11:00
12:00
1:00
2:00
3:00
4:00
5:00
6:00
7:00
8:00
Item
High Range Concentration
History Size: 1 hour (Statistics Generated For Plot Duration)
Plot filter: None
Alt plot filter: None
Filter join: Off
Flyer filter: None
Plot Data Type
PPM Value
Minimum
-1.264
Maximum
438.924
Average
24.790
Std Dev
92.225

Figure 17

ION MOBILITY SPECTROMETRY ANALYZER FOR DETECTING PEROXIDES

CROSS-REFERENCE TO RELATED APPLICATIONS

[0001] This application claims priority under 35 U.S.C. 119(e) to U.S. Provisional Patent Application Nos. 60/952,669, filed Jul. 30, 2007, 60/953,879, filed Aug. 3, 2007, and 60/984,804 filed Nov. 2, 2007, each of which are hereby incorporated by reference in there entirety to the extent not inconsistent with the disclosure herein.

BACKGROUND OF INVENTION

[0002] Recent developments in ion mobility spectrometry have made this technique a widely applicable and powerful analytical tool for detection and characterization of a broad class of molecules. Ion mobility spectrometric analysis provides one of the most universally applicable analysis methods, as it is applicable to almost any species capable of forming an ion in the gas phase. In addition, ion mobility spectrometry methods provide highly selective and sensitive detection (e.g., parts per trillion for some species). Accordingly, these methods are especially attractive for quantitative analysis of analyte compounds present at low concentrations in complex mixtures. Further, ion mobility spectrometry methods do not require high vacuum conditions, in contrast to mass spectrometry techniques and, therefore, are compatible with a wide range of detection environments and operating conditions. As a result of this unique combination of beneficial attributes, ion mobility spectrometry currently provides a versatile detection platform useful for a range of important applications including clean room monitoring, trace gas detection of hazardous industrial chemicals, explosives and nerve agents, and monitoring for chemical processing applications (e.g., the production of pharmaceuticals, reagent chemicals etc).

[0003] An ion mobility spectrometer (IMS) typically comprises an ionization region, a separation region (e.g., a drift cell) and an ion detector. Analytes in a sample are provided to the ionization region and interact with an ionization source, such as a radioactive source, UV source, or corona discharge source, thereby generating analyte ions typically via a complex series of gas phase ion-neutral and ion-ion reactions. In many cases analyte ions are actually complexes, clusters and/or aggregates derived from the analyte(s) of interest that provide an IMS signal useful for identifying and characterizing (e.g., measuring the concentration of) analyte(s) in the sample. Analyte ions are subsequently introduced into a drift cell held at or near atmospheric pressure, for example using pulsed extraction provided by an ion injection shutter or grid, and are accelerated in the drift tube by application of an electric potential. In the drift tube, analyte ions and other ions in the system are exposed to a counter flow of drift gas and undergo physical separation on the based of their ion mobility. The separated analyte ions are subsequently detected using an ion detector such as a microchannel plate or Faraday cup detector.

[0004] As the drift time of ions through the drift tube depends on their electric charge, size and shape, IMS analysis provides a means of reliably identifying the presence of, and measuring the concentration of analytes present in the sample. Specific analyte selective IMS analyzers commonly utilize gated detection at preselected times corresponding to the drift times of analyte ions of interest. Alternatively, broad band IMS instruments are capable of measuring arrival times of analyte ions continuously as a function of time, thereby generating an IMS spectrum characterizing a plurality of components of a sample. A range of IMS analyzers have been developed that operate in positive ion mode, negative ion mode or dual ion mode, depending on the electric charge of the analyte ions analyzed and detected by the system.

[0005] Given that analytes are analyzed and detected on the basis of their corresponding analyte ions, the ion formation process significantly impacts the capability of IMS methods and systems for detecting and characterizing specific gas phase analytes. For example, the efficiency in which analyte ions are formed from a given analyte and the stability of the analyte ions formed at least in part determines detection sensitivity. In addition, the selectivity of IMS techniques at least in part is determined by the degree of separation between the drift time(s) corresponding to analyte ions and the drift times of background ions formed by ionization of the carrier gas (es), drift gas(es), impurities and/or other species present in the sample. It is known, for example, that generation of background ions in the IMS system having drift times similar to those of analyte ions can mask the IMS signal(s) used to detect and characterize an analyte of interest. This source of inference may result in false positive readings that degrade overall performance, and is particularly significant for applications involving the identification and detection of analytes present in a sample at low concentrations.

[0006] To overcome these limitations, a range of ionization strategies have been developed for detecting specific analytes. Many of these strategies involve introduction of dopant molecules (i.e., dopants) into the ionization region that affect the ion-molecule reaction chemistry and charge state distributions of ions generated in the IMS analyzer. In some of these strategies, dopants are provided to the IMS system having properties, such as electric charge affinities or proton affinities, that result in a redistribution electric charge by removing charge from the potentially interfering ions via charge transfer or proton transfer reactions. Charge redistribution in these techniques is useful for reducing potential interference by eliminating or minimizing interfering peaks in the IMS spectrum. Ionization strategies have also been developed wherein dopants are provided that selectively adjust the drift times of analyte ions so as to enhance their selective detection. In some systems, dopants are introduced that selectively adjust the compositions or charge states of analyte ions formed in the ionization region so as to provide drift times that are easily distinguished from those of background ions generated in the IMS system. For example, dopants and/or ions derived from dopants may participate in associative reactions with analyte ions or induce fragmentation of analyte ions so as to provide a desirable shift in drift time. In other ionization strategies, dopants are provided to the IMS system that shift the drift times of background ions away from those of analyte ions derived from analytes of interest in the sample. This dopant strategy also provides a means of minimizing and/or avoiding overlap of peaks in the mobility spectrum so as to enhance selectivity and sensitivity of ion mobility spectrometry methods.

[0007] Given the potential benefits provided by ionization strategies involving dopants, substantial research is currently directed toward developing dopants effective for enhancing the selectivity and sensitivity of ion mobility spectrometry. The potential applicability of IMS methods and systems for a

wide range of detection and sensing application continues to provide motivation for identifying and characterizing new dopant compounds and ionization strategies useful for detecting specific analytes of interest.

[0008] U.S. Pat. No. 5,032,721 discloses an IMS analyzer wherein dopant is provided to enhance selectivity for detecting acid gas analytes. An IMS analyzer is described using a purified air carrier gas wherein addition of dopant is reported to shift the drift times of background ions generated from components of the carrier gas so as to avoid interference in the detection of analyte ions derived from the acid gas analytes. Addition of the dopant in the disclosed system is reported to not appreciable change the drift times of analyte ions generated from the acid gas analytes. The shift in the drift times of ions in the analyzer caused by the addition of dopant is reported to minimize interferences arising from the use of air as a carrier gas in the IMS analyzer. The dopants disclosed in this reference include methyl salicylate and 2-hydroxyacetonephenone, which are reported as useful for providing selective detection of strong acids, such as hydrogen fluoride gas and hydrogen chloride gas.

[0009] International Patent Publication No. WO 2006/123107 discloses IMS analyzers and methods using a 2,4-pentanedione dopant. Introduction of a 2,4-pentanedione dopant is reported as effective for shifting the position of an ion peak corresponding to a substance of interest away from peaks corresponding to background ions generated in the IMS analyzer. In addition, introduction of a 2,4-pentanedione dopant is reported as effective for shifting the position of peaks corresponding to background ions generated in the IMS analyzer away from an ion peak(s) corresponding to an analyte of interest. The dopant disclosed in this reference is reported as useful for enhancing and improving identification and quantification of a very wide class of compounds including toxic industrial chemicals, such as acid gases, halogens, phosgene, and hydrogen cyanide. The reference also discloses that it is believed that the 2,4-pentanedione dopant would be effective in detecting nitrogen compounds and compounds present in the breath of mammals, such as nitrous oxide, nitric oxide and hydrogen peroxide.

[0010] International Patent Publication No. WO 2007/085898 discloses IMS analyzers and methods using a class of amide dopants. The disclosed amide dopants are reported to be useful for identification of a range of analytes including peroxide-based explosives including hexamethylenetriperoxidediamine (HMTD) and triacetone triperoxide (TATP). Dopants exemplified in this publication include 2-methylpropionamide and isobutyramide.

[0011] It will be appreciated from the foregoing that IMS analyzers and methods are currently needed for a range of sensing and detection applications. IMS analyzers and methods are needed providing enhanced sensitivity for detecting and characterizing analytes present at very low concentrations (e.g., parts per billion and/or parts per trillion) in samples. In addition, IMS analyzers and methods are needed providing enhanced selectivity for detecting and characterizing specific gas phase analytes provided in samples comprising complex mixtures. Further, IMS analyzers and methods are needed having a useful dynamic range so as to be able to detect analytes present in samples in widely varying concentrations.

SUMMARY OF THE INVENTION

[0012] The present invention provides IMS analyzers and methods for detecting, identifying, and characterizing (e.g., measuring the concentration of) peroxides in samples. In an embodiment, methods and systems of the present invention utilize dopant strategies, and optionally sample inlet conditions, providing an enhancement in selectivity and sensitivity for the detection of peroxide analytes relative to conventional IMS analyzers. The present IMS analyzers and methods are versatile and enable selective detection of a broad class of peroxides and derivatives thereof, including hydrogen peroxide, hydroperoxides, organic peroxides and derivatives thereof. Methods and systems of the invention also are capable of accurate peroxide measurements over a large effective dynamic range. Systems and methods of some aspects, for example, provide detection and characterization peroxides over a concentration range at low as a few parts per billion (ppb) to a high as 1000's of parts per million (ppm), and are capable of real time detection and characterization of peroxides with fast response times on the order of milliseconds for some sampling conditions. Methods and systems of the present invention are also capable of accurate and stable calibration, optionally via an automated, on board calibration system.

[0013] In an aspect, the present IMS peroxide detection systems and methods provide enhanced sensitivity and selectivity by minimizing, or entirely eliminating, sources of interference arising from background ions generated from carrier gases, drift gases and/or impurities present in a sample. A number of strategies are useful in the present invention for suppressing interference from ions generated from water vapor such as: (i) use of a sample introduction interface providing preferential transport of peroxides into the system relative to water vapor, (ii) addition of dopant(s) to the system capable of modifying the drift times of potentially interfering ions away from those of peroxide analyte ions via charge transfer, charge scavenging, complex formation and/or cluster formation reactions, and (iii) addition of dopant(s) to the system capable of modifying the drift times of peroxide analyte ions away from those of potentially interfering ions via charge transfer, complex formation and/or cluster formation reactions. In an embodiment of the present invention, dopant provided to the analyzer scavenges electrical charge from interfering ions generated from water vapor in the analyzer. IMS methods and analyzers of some embodiments use a combination of sample introduction via a selectively permeable hydrophobic membrane and the addition of specific dopant(s) to achieve sampling and ionization conditions that effectively suppress interfering IMS signals corresponding to ions derived from water vapor in the sample. Ionization and detection conditions accessed by this aspect of the invention, therefore, provide a distinctive IMS signal(s) corresponding to peroxide analyte(s) that is easily identified, quantified and distinguished from IMS signals corresponding to other ions derived from water vapor and/or other impurities in the system. This feature of the present invention is particularly beneficial for detection and sensing applications in environments having a significant water component, such as monitoring of peroxides during aseptic processing, ambient air monitoring, and in homeland security applications for detection of peroxide-based explosives and/or precursors of peroxide-based explosives. This feature of the present invention is also useful for enhancing sensitivity and selectivity in IMS analyzers using air as a carrier gas and/or drift gas given the significant and variable concentrations of water vapor commonly present in air.

[0014] In an aspect, the present invention provides an ion mobility spectrometry analyzer for detecting peroxides analytes in a sample. An ion mobility spectrometry (IMS) analyzer of the present invention comprises: an inlet, a source of dopant, an ionization region, a separation region, and a detector. The inlet is provided in fluid communication with the ionization region and is configured to provide peroxide analytes to the analyzer. The source of dopant is provided to introduce dopant into analyzer, and preferably for some applications provides a preselected concentration of dopant in the ionization and/or separation regions of the analyzer. The ionization region has an ionization source for generating analyte ions from peroxides analytes and, optionally dopant (s), provided to the analyzer.

[0015] In an embodiment, the dopant is a substituted aryl compound or a substituted cyclic diene; wherein the substituted aryl compound or the substituted cyclic diene has at least one substituent selected from the group consisting of a hydroxyl group, a carbonyl group, an aldehyde group, an ester group, a carboxylic acid group and a carbonate ester group. Effective dopants for negative mode IMS detection of peroxide analytes include, but are not limited to, a substituted benzene derivative having at least one substituent selected from the group consisting of a hydroxyl group, a carbonyl group, an aldehyde group, an ester group, a carboxylic acid group and a carbonate ester group. In an embodiment of the present invention, the dopant is a substituted or unsubstituted phenol, or a substituted or unsubstituted quinone. In an embodiment wherein the formation and/or detection of potentially interfering ions is minimized the dopant provided to the IMS analyzer is methyl salicylate or 2-hydroxyacetophenone.

[0016] In an embodiment, the inlet is a hydrophobic membrane, for example, having a composition providing preferential permeability and transport into the analyzer of peroxide analytes relative to water vapor. This sampling interface provides effective sampling and detection of peroxides while minimizing the abundance of water vapor introduced into the analyzer. Optionally, the inlet is positioned such that a flow of carrier gas(es) facilitates transport of peroxide analytes into the ionization and/or separation regions of the analyzer. The inlet, source of dopant, and ionization region are provided in fluid communication with each other such that sample and dopant are provided to the analyzer and undergo ionization in the ionization region, thereby generating analyte ions corresponding to peroxide analytes.

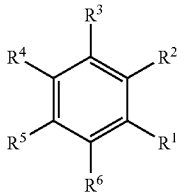
[0017] The separation region of the analyzer is provided in fluid communication with the ionization region so as to receive and separate analyte ions from the ionization source on the basis of ion mobility. Useful separation regions of this aspect of the present invention include an IMS cell, such as drift tube or other type of time-of-flight chamber. Optionally, the analyzer of the present invention further comprises a means of extracting ions provided between the ionization region and separation region, for example charge particle optics, such as an ion injection shutter or grid. A detector is provided in fluid communication with the separation region for receiving and detecting peroxide analyte ions, and optionally dopant ions (expressly including monomers, dimers, trimers, clusters and fragments thereof), separated on the basis of ion mobility. In an embodiment, the detector is gated at preselected drift times corresponding to analyte ions generated from the peroxides and, optionally, ions generated from dopant(s). In some embodiments, the present invention provides negative mode IMS methods and analyzers operated in normal mode or enhanced mode wherein negatively charged peroxide analyte ions are generated in the ionization region, separated on the basis of mobility and detected.

[0018] Dopants useful in the present invention have compositions, chemical properties and/or physical properties that provide sensitive and selective detection of peroxide analytes in a sample. The addition of dopant(s) in the present systems enhances selective and sensitive detection of peroxides by accessing ionization, separation and detection conditions wherein the signature drift times of analyte ions provide IMS signal(s) corresponding to peroxide analytes that are easily identified, detected and quantified. In some embodiments, dopant(s) provided to the IMS analyzer reduces the magnitude, or entirely eliminates, IMS signals corresponding to potentially interfering ions resulting from water vapor and having drift times similar to that of peroxide analyte ions. Elimination of interfering signals is achieved in some embodiment by providing dopants to the IMS analyzer that participate in chemical reactions, such as charge transfer reactions, complex formation reactions and/or clustering reactions, capable of neutralizing and/or shifting the drift times of potentially interfering ions derived from water vapor away from those of analyte ion(s) corresponding to peroxides. Addition of dopant in these embodiments shifts the drift times of potentially interfering ions so they do not obscure the detection, identification and quantification of peroxide analyte ions.

[0019] Dopants that are chemically stable and can be provided to the ionization region and/or separation region in preselected amounts and at preselected concentrations are particularly attractive in IMS methods and analyzers of the present invention because they enable highly stable detection conditions and sensitivities. In some embodiments, dopants of the present invention have charge affinities larger than that of background ions generated from carrier gas(es), drift gas (es) and impurities in the analyzer. This aspect allows for at least partial neutralization and/or reduction of background ions by charge scavenging processes involving dopants and reagent ions in the ionization and/or separation regions. The present invention also includes, however, methods and systems wherein dopants are provided to the IMS analyzer that are capable of participating in chemical reactions, such as complex formation reaction and/or clustering reactions that provide a shift of the drift times of analyte ions away from those of potentially interfering ions, thereby enhancing detection selectivity and sensitivity. The present invention also includes methods and systems wherein dopants are provided to the IMS analyzer in sufficient concentrations such that they maintain and/or stabilize clusters and/or complexes corresponding to analytes in the separation region, thereby improving the overall sensitivity and reliability of the measured spectrum.

[0020] In an embodiment, the dopant provided to the analyzer is a substituted benzene derivative having the formula:

(F1)



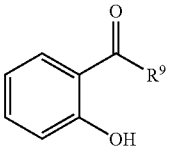
[0021] wherein each of R^1, R^2, R^3, R^4, R^5, and R^6, is independently selected from the group consisting of a hydrogen, a halogen, CN, OR, COOR, OCOOR, COR, $N(R)_2$, SR,

SO_2R, SOR, a substituted or unsubstituted C_1-C_{20} alkyl group, a substituted or unsubstituted C_2-C_{20} alkenyl group, a substituted or unsubstituted C_2-C_{20} alkynyl group, a substituted or unsubstituted C_1-C_{20} alkoxy group, and a substituted or unsubstituted C_4-C_{20} aryl group; wherein each R, independent of any other R in any listed group, is selected from H, a substituted or unsubstituted C_1-C_{20} alkyl group, a substituted or unsubstituted C_4-C_{20} aryl group, a substituted or unsubstituted C_2-C_{20} alkenyl group, a substituted or unsubstituted C_2-C_{20} alkynyl group, and a substituted or unsubstituted C_3-C_{20} acyl group, and wherein at least one of R^1, R^2, R^3, R^4, R^5, and R^6 is a hydroxyl group, a carbonyl group, an aldehyde group, an ester group, a carboxylic acid group or a carbonate ester group

[0022] In an embodiment, for example, the dopant is a phenol having formula F1 wherein at least one of R^1, R^2, R^3, R^4, R^5, and R^6 is —OH. In an embodiment, for example, the dopant is a compound having formula F1 wherein R^1 is —OR and a R^2 is COOR, optionally where R is H, CH_3, CH_2CH_3, or $CH_2CH_2CH_3$, and optionally wherein R^3, R^4, R^5, and R^6 are each H. In an embodiment, for example, the dopant is a compound having formula F1 wherein R^1 is —OR and a R^2 is COR, optionally where R is H, CH_3, CH_2CH_3, or $CH_2CH_2CH_3$, and optionally wherein R^3, R^4, R^5, and R^6 are each H. In an embodiment, for example, the dopant is a compound having formula F1 wherein R^1 is OH and a R^2 is $COOCH_3$, optionally wherein R^3, R^4, R^5, and R^6 are each H.

[0023] In an embodiment, the dopant provided to the analyzer is a substituted phenol having a carbonyl substituent, the dopant having formula:

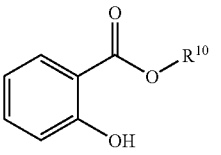
(F2)



[0024] wherein R^9 is selected from the group consisting of a hydrogen, a halogen, CN, OR, COOR, OCOOR, COR, $N(R)_2$, SR, SO_2R, SOR, a substituted or unsubstituted C_1-C_{20} alkyl group, a substituted or unsubstituted C_2-C_{20} alkenyl group, a substituted or unsubstituted C_2-C_{20} alkynyl group, a substituted or unsubstituted C_1-C_{20} alkoxy group, and a substituted or unsubstituted C_4-C_{20} aryl group; and wherein each R, independent of any other R in any listed group, is selected from H, a substituted or unsubstituted C_1-C_{20} alkyl group, a substituted or unsubstituted C_4-C_{20} aryl group, a substituted or unsubstituted C_2-C_{20} alkenyl group, a substituted or unsubstituted C_2-C_{20} alkynyl group, and a substituted or unsubstituted C_3-C_{20} acyl group. In an embodiment, for example, the dopant is a compound having formula F2 wherein R^9 is a hydrogen or a C_1-C_{10} substituted or unsubstituted alkyl group. In an embodiment, for example, the dopant is a compound having formula F2 wherein R^9 is H, CH_3, CH_2CH_3, or $CH_2CH_2CH_3$. In an embodiment, for example, the dopant is a compound having formula F2 wherein R^9 is CH_3 or OCH_3.

[0025] In an embodiment, the dopant provided to the analyzer is a substituted phenol having an ester substituent, the dopant having the formula:

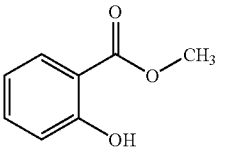
(F3)



wherein R^{10} is selected from the group consisting of a hydrogen, a halogen, CN, OR, COOR, OCOOR, COR, $N(R)_2$, SR, SO_2R, SOR, a substituted or unsubstituted C_1-C_{20} alkyl group, a substituted or unsubstituted C_2-C_{20} alkenyl group, a substituted or unsubstituted C_2-C_{20} alkynyl group, a substituted or unsubstituted C_1-C_{20} alkoxy group, and a substituted or unsubstituted C_4-C_{20} aryl group; and wherein each R, independent of any other R in any listed group, is selected from H, a substituted or unsubstituted C_1-C_{20} alkyl group, a substituted or unsubstituted C_4-C_{20} aryl group, a substituted or unsubstituted C_2-C_{20} alkenyl group, a substituted or unsubstituted C_2-C_{20} alkynyl group, and a substituted or unsubstituted C_3-C_{20} acyl group. In an embodiment, for example, the dopant is a compound having formula F3 wherein R^{10} is a hydrogen or a C_1-C_{10} substituted or unsubstituted alkyl group. In an embodiment, for example, the dopant is a compound having formula F3 wherein R^{10} is H, CH_3, CH_2CH_3, or $CH_2CH_2CH_3$.

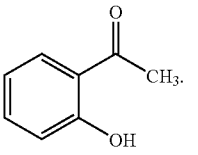
[0026] In a specific embodiment, for example, the dopant is methyl salicylate:

(F4)



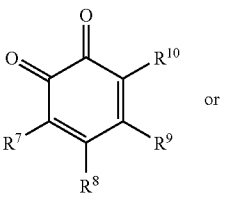
[0027] or is 2-hydroxyacetophenone:

(F5)



[0028] In an embodiment, the dopant provided to the analyzer is a substituted or unsubstituted quinone having the formula:

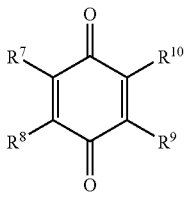
(F6)



or

-continued

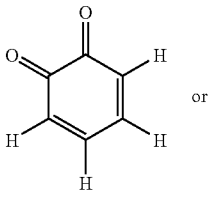
(F7)



[0029] wherein each of R^7, R^8, R^9 and R^{10} is independently selected from the group consisting of: a hydrogen, a halogen, CN, OR, COOR, OCOOR, COR, $N(R)_2$, SR, SO_2R, SOR, a substituted or unsubstituted C_1-C_{20} alkyl group, a substituted or unsubstituted C_2-C_{20} alkenyl group, a substituted or unsubstituted C_2-C_{20} alkynyl group, a substituted or unsubstituted C_1-C_{20} alkoxy group, and a substituted or unsubstituted C_4-C_{20} aryl group; and wherein each R, independent of any other R in any listed group, is selected from H, a substituted or unsubstituted C_1-C_{20} alkyl group, a substituted or unsubstituted C_4-C_{20} aryl group, a substituted or unsubstituted C_2-C_{20} alkenyl group, a substituted or unsubstituted C_2-C_{20} alkynyl group, and a substituted or unsubstituted C_3-C_{20} acyl group. In an embodiment, for example, the dopant is a compound having formula F6 or F7 wherein each of R^7, R^8, R^9 and R^{10} is independently selected from the group H, CH_3, CH_2CH_3, or $CH_2CH_2CH_3$. In an embodiment, for example, the dopant is a compound having formula F6 or F7 wherein each of R^7, R^8, R^9 and R^{10} is H.

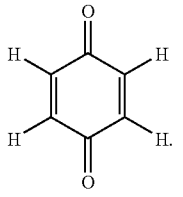
[0030] In an embodiment, the dopant provided to the analyzer is an unsubstituted quinone having the formula:

(F8)



or

(F9)



[0031] In an embodiment, the source of dopant provides a preselected concentration of dopant(s) in the analyzer. In an embodiment, for example, the source of dopant provides a concentration of dopant in the ionization region and/or separation region selected over the range of 1 ppm to 500 ppm, preferably for some applications selected over the range of 1 ppm to 100 ppm, and preferably for some applications selected over the range of 20 ppm to 50 ppm. Dopants in the present invention can be mixed with peroxide analytes prior to introduction into the ionization region, or alternatively may be mixed with peroxide analytes in the ionization region and/or separation region. In an embodiment, dopant is introduced to the separation region and, optionally conveyed to the ionization region by the flow of drift gas. In some embodiments, dopants are introduced with the drift gas to the separation region, optionally to provide dopant in the separation region at an elevated concentration (e.g., 10 ppm to 500 ppm).

[0032] The present IMS analyzers and methods may use a single dopant or a plurality of dopants. Use of methyl salicylate is particularly beneficial as it provides highly selective, stable and sensitive detection of peroxides. Methyl salicylate is also chemically stable, nontoxic in low concentrations and can be easily provided to the ionization or separation regions of an IMS analyzer in accurately preselected rates and at preselected concentrations. Useful sources of dopants in the present invention include, but are not limited to, permeation tube sources, molecular sieve sources, chemical reservoir, temperature-generated sources, and/or evaporative sources.

[0033] Incorporation of an inlet comprising a hydrophobic membrane provides systems and methods of the present invention providing enhanced selectivity and sensitivity by suppressing the amount of water vapor in the sample that is introduced to the analyzer. In the context of this description, "hydrophobic membrane" refers to a sampling interface that is at least semipermeable to hydrogen peroxide analytes and that has at least a partial hydrophobic character. Hydrophobic membranes useful in the present invention include, but are not limited to, a "coated membrane" having hydrophobic properties. Coated membranes useful in the present invention include a semipermeable membrane that is coated with one or more hydrophobic materials, layers and/or coatings.

[0034] Hydrophobic membranes of the present invention include microporous membranes having one or more hydrophobic coatings. In a specific embodiment, for example, the hydrophobic membrane is a microporous membrane having pores sizes ranging from 0.01 μm to 10 μm coated with a hydrophobic coating. Hydrophobic membranes of the present IMS analyzers may have a range of physical dimensions. In an embodiment, a hydrophobic membrane of the present invention has a thickness selected from the range of 0.1 millimeter to 10 millimeters. In an embodiment, a hydrophobic membrane of the present invention has an internal and/or external surface with an area selected over the range of 10 mm^2 to 100 cm^2.

[0035] In an embodiment, the hydrophobic membrane is a Teflon® membrane, for example a microporous Teflon membrane, coated with a hydrophobic coating. Specific embodiments of the present invention include use of a Goretex® membrane coated with a hydrophobic coating. The present invention includes, however, membranes having a composition other than Teflon® including, but not limited to, dimethylsilicone, polypropylene, polydimethyl siloxane, Nylon®, polytetrafluoroethylene, polyvinylidene difluoride and/or acrylic copolymer.

[0036] Hydrophobic coatings of membranes of the present invention is useful for enhancing the capability of the analyzer for minimizing the amount of water vapor introduced into the ionization region. Hydrophobic coatings may be provided on the internal and/or external surface of the membrane, for example, by drip coating, spin coating, spray coating and/or deposition coating methods. Useful coatings for hydrophobic membranes of the present invention include, silicone hydrophobic coatings, such as silane coatings, siloxane coatings (e.g., polydimethylsiloxane coatings), fluorocarbon coatings, and others known in the art. In an embodiment, the hydrophobic membrane comprises an OV-101

coating. In some embodiments, useful coatings for hydrophobic membranes of the present invention have thicknesses selected from the range of 10 microns to 100 microns. The present invention includes ion mobility spectrometry analyzers comprising a plurality of coatings provided to a semipermeable membrane, such as a microporous membrane.

[0037] The composition, physical properties and/or chemical properties of the hydrophobic membrane is selected in some embodiments to provide preferential diffusivity and/or permeability of peroxide analytes relative to water vapor. In an aspect, the hydrophobic membrane of the present invention provides a means for purifying sample introduced into the ion mobility spectrometry analyzer, for example, by preventing transmission of at least a portion of water vapor in the sample. This aspect of the present invention can be accomplished using a hydrophobic membrane having a composition providing significantly different permeation rates for peroxide analytes and water vapor, such as a permeation rate for peroxide analyte that is at least 2 times greater than the permeation rate of water vapor, and in some embodiments as a permeation rate for peroxide analytes that is at least 5 times greater than the permeation rate of water vapor. Hydrophobic membranes useful in the present invention may also have physical properties such that they at least partial prevent transmission of particulate material suspended in the sample into the ion mobility spectrometry analyzer.

[0038] Hydrophobic membranes of the present invention may optionally be provided in a configuration wherein an internal surface of the membrane is in contact with a flow of carrier gas(es) so as to facilitate transport of peroxides entering the analyzer into the ionization region. In a specific embodiment, for example, the hydrophobic membrane has an external surface and an internal surface; wherein the sample is provided in contact with the external surface of the hydrophobic membrane such that one or more peroxides in the sample diffuse through the membrane. A source of carrier gas may further be provided in fluid communication with the membrane so as to generate a flow of carrier gas that contacts or "sweeps" the internal surface of the membrane. This membrane inlet configuration is useful to ensure substantially all (e.g., at least 75%) of the peroxide passing through the membrane is transported to the ionization region.

[0039] Optionally, IMS analyzers of the present invention may further comprise a calibration system and/or calibration verification system. Useful calibrants for IMS systems and methods of the present invention are preferably chemically stable and generate a calibrant ion having a drift time that is close (e.g., within 10%) to that of the drift times of analyte ions generated from peroxide analytes. This results in a calibration IMS peak in the same window as the peak(s) generated from peroxide analyte ions. In an embodiment, a calibration system and/or verification system is provided comprising a source of acetic acid in fluid communication with the ionization region of the IMS analyzer. Use of acetic acid is particularly useful for analyzers and methods for detecting hydrogen peroxide (H_2O_2) as the ion peak drift time corresponding to acetic acid analyte is very similar of that of hydrogen peroxide. In addition, acetic acid is chemically stable, nontoxic and can be provided accurately in known amounts, for example using convenient sources such as a permeation tube source. In this embodiment of the present invention, a calibration source is provided that is capable of introducing a known amount of acetic acid into the ionization region. Measuring the IMS signal upon introduction of a known amount of acetic acid allows the sensitivity and/or signal response characteristics of the IMS analyzer for hydrogen peroxide analytes to be quantitatively assessed and/or verified. The present invention includes IMS analyzers and methods providing fully or partially automated calibration and/or calibration verification systems.

[0040] Optionally, IMS analyzers of present invention further comprise a means for diluting the gas sample containing peroxide analytes prior to analysis, for example comprising an internal dilution module. Incorporation of a dilution means is beneficial in some embodiments so as to enhance the upper end of the dynamic range of the present IMS analyzers. In some embodiments, the present invention provides IMS analyzers having a means for diluting the gas sample that allows accurate measurements for gas phase peroxide concentrations as high as 1000's of ppms

[0041] IMS methods and analyzers of the present invention provide a versatile detection platform for detecting, identifying and characterizing a range of hydrogen peroxide, hydroperoxide and organic peroxide analytes, including but not limited to H_2O_2, acetone peroxide, methyl ethyl ketone peroxide, benzoyl peroxide, hexamethylenetriperoxidediamine, and triacetone triperoxide.

[0042] IMS analyzers and methods of the present invention are particularly useful for monitoring hydrogen peroxide concentrations during aseptic processing, for example for clean room processing isolation in pharmaceutical and biological materials production and processing. Advantages of the present methods and systems include an effective dynamic range that enables continuous hydrogen peroxide monitoring during the conditioning phase, the sterilization (or decontamination phase) and the aeration phase wherein hydrogen peroxide levels typically vary from a few ppbs to 1000s of ppms. The present methods and systems also provide stable detection conditions over the long time domains (e.g. hours) involved in aseptic processing.

[0043] IMS analyzers and methods of the present invention are particularly useful for identifying and detecting peroxides that may comprise components and/or precursors of explosives. This aspect of the present invention is attractive for a range of homeland security applications. Advantages of the present methods and systems for this application include the capability to detect a range of peroxides that are common compounds and/or precursors of explosives and the capability to detect peroxides at very low concentrations.

[0044] In another aspect, the present invention provides a method for selectively detecting one or more peroxide analytes in a sample comprising the steps: (i) providing an ion mobility spectrometry analyzer having an inlet, ionization region, separation region and detector; (ii) passing at least a portion of the peroxide analytes through the inlet of the analyzer into the ionization region of the analyzer; (iii) providing dopant to the ionization region, separation region or both of the analyzer, wherein the dopant is a substituted aryl compound or a substituted cyclic diene; wherein the substituted aryl compound or the substituted cyclic diene has at least one substituent selected from the group consisting of a hydroxyl group, a carbonyl group, an aldehyde group, an ester group, a carboxylic acid group and a carbonate ester group; (iv) generating analyte ions from the peroxide analytes in the ionization region; (v) passing the analyte ions through a separation region of the ion mobility spectrometry analyzer, the separation region provided in fluid communication with the ionization source, wherein the analyte ions are separated on the

basis of ion mobility; and (vi) detecting the analyte ions separated on the basis of ion mobility using a detector provided in fluid communication with the separation region. In a method of the present invention, the dopant is a substituted benzene derivative having at least one substituent selected from the group consisting of a hydroxyl group, a carbonyl group, an aldehyde group, an ester group, a carboxylic acid group and a carbonate ester group. In a method of the present invention, the dopant is a substituted or unsubstituted phenol, such as methyl salicylate or 2-hydroxyacetophenone, or a substituted or unsubstituted quinone. In some methods, dopant is provided to said ionization region, separation region or both at a concentration selected from the range of 1 ppm to 100 ppm. In some embodiments, the inlet is a hydrophobic membrane that at least partially prevents transmission of water vapor in the sample into the ionization region of the analyzer. In some embodiments, the step of providing dopant to the separation region suppresses interference from ions generated from water in the analyzer. In some embodiments, the step of providing dopant to the ionization and/or separation regions results in detection conditions wherein analyte ions have drift times that are distinguishable from the drift times of ions generated from water in the analyzer. As will be understood by one having ordinary skill in the art of IMS detection and sensing, any of the IMS detector embodiments and features thereof described herein can be used with the present methods.

[0045] In another aspect, the present invention provides a method of suppressing interference from water vapor in an ion mobility spectrometry analyzer comprising the steps: (i) providing an ion mobility spectrometry analyzer having an inlet, ionization region, separation region and detector; (ii) passing at least a portion of a sample having peroxide analytes through the inlet of the analyzer into the ionization region of the analyzer; (iii) providing dopant to the ionization region, separation region or both of the analyzer, wherein the dopant is a substituted aryl compound or a substituted cyclic diene; wherein the substituted aryl compound or the substituted cyclic diene has at least one substituent selected from the group consisting of a hydroxyl group, a carbonyl group, an aldehyde group, an ester group, a carboxylic acid group and a carbonate ester group; wherein the dopant provided to the ionization region, separation region or both of the analyzer suppresses interference from water vapor in the ion mobility spectrometry analyzer. In a method of the present invention, the dopant is a substituted benzene derivative having at least one substituent selected from the group consisting of a hydroxyl group, a carbonyl group, an aldehyde group, an ester group, a carboxylic acid group and a carbonate ester group. In a method of the present invention, the dopant is a substituted or unsubstituted phenol, such as methyl salicylate or 2-hydroxyacetophenone, or a substituted or unsubstituted quinone. In some methods, dopant is provided to said ionization region, separation region or both at a concentration selected from the range of 1 ppm to 100 ppm. In some embodiments, the inlet is a hydrophobic membrane provided to at least partially prevent transmission of water vapor in the sample into the ionization region of the analyzer. In some embodiments, the dopant provided to the analyzer scavenges electrical charge from interfering ions generated from water in the analyzer, thereby suppressing interference from water vapor in the ion mobility spectrometry analyzer. In some embodiments, the step of providing dopant to the ionization and/or separation regions results in detection conditions wherein the peroxide analytes generate analyte ions having drift times that are distinguishable from the drift times of ions generated from water in the analyzer. As will be understood by one having ordinary skill in the art of IMS detection and sensing, any of the IMS detector embodiments and features thereof described herein can be used with the present methods.

[0046] Without wishing to be bound by any particular theory, there can be discussion herein of beliefs or understandings of underlying principles relating to the invention. It is recognized that regardless of the ultimate correctness of any mechanistic explanation or hypothesis, an embodiment of the invention can nonetheless be operative and useful.

BRIEF DESCRIPTION OF THE DRAWINGS

[0047] FIG. **1**A provides a schematic diagram illustrating an ion mobility spectrometry analyzer of the present invention useful for detecting, identifying and/or characterizing peroxides, such as hydrogen peroxide, in samples.

[0048] FIG. **1**B provides a schematic diagram illustrating an alternative IMS analyzer configuration of the present invention. As shown in FIG. **1**B, the inlet system for introducing the sample differs from that shown in FIG. **1**A.

[0049] FIG. **1**C provides a schematic diagram illustrating an alternative IMS analyzer configuration. As shown, the inlet and exhaust are positioned similarly to that shown in FIG. **1**A, but without a membrane.

[0050] FIG. **2** provides an IMS time of flight spectrum for the detection of hydrogen peroxide obtained using the present IMS analyzer with a methyl salicylate dopant

[0051] FIG. **3** provides an overlap plot corresponding to a plurality of measurements of the IMS spectrum for peroxide detection under the same sample and analyzer conditions. The spectra shown in FIG. **3** indicate that the present IMS analyzer provides very reproducible spectra.

[0052] FIG. **4** provides a plot of hydrogen peroxide concentration versus IMS response as expressed by observed peak height ratio.

[0053] FIG. **5** provides a plot of instrument response expressed in units of hydrogen peroxide concentration as a function of time (min) for the introduction of a 10 ppm sample of hydrogen peroxide.

[0054] FIG. **6** provides a plot of instrument response expressed in units of hydrogen peroxide concentration verse time (min) for the introduction of a 600 ppm sample of hydrogen peroxide.

[0055] FIG. **7** shows experimental results for a stability test of the present IMS analyzer.

[0056] FIG. **8** provides a plot of the signal-to-noise ratio as a function of time for an IMS analyzer of the present invention for conditions of no gas phase gas analyte.

[0057] FIG. **9** provide a typical 10 ppm span calibration check using on-board calibration (OBC).

[0058] FIG. **10** provides a comparison plot showing experimental data for the present IMS analyzer, electrochemical cell and NIR monitor for the high hydrogen peroxide conditions of the sterilization phase. Peroxide concentration is plotted as a function of time (min).

[0059] FIG. **11** provides a plot of IMS signal (in units of peroxide concentration) as a function of time (min) for experimental conditions wherein the inlet tube was cut at the isolator.

[0060] FIG. **12** provides experimental results comparing a NIR monitor, an electrochemical monitor, and the present

IMS analyzer for monitoring hydrogen peroxide during conditioning, sterilization and aeration phases.

[0061] FIG. **13** provides an expanded view of the experimental data show in FIG. **11** corresponding to the aeration cycle.

[0062] FIG. **14** provides a comparison of hydrogen peroxide concentrations measured by the present IMS analyzer and the electrochemical cell during the aeration phase.

[0063] FIG. **15** provides a plot of hydrogen peroxide concentrations determined using the present IMS peroxide analyzer for filing isolator conditioning and sterilization. In FIG. **15** peroxide concentration is plotted as a function of time (min).

[0064] FIG. **16** provides a plot of hydrogen peroxide concentrations determined using the present IMS peroxide analyzer for monitoring transfer isolator during conditioning, sterilization, and aeration. In FIG. **16**, hydrogen peroxide concentrations are plotted as a function of time (min).

[0065] FIG. **17** provides a plot of hydrogen peroxide concentrations determined using the present IMS peroxide analyzer for monitoring completion of aeration cycle on transfer isolator. In FIG. **17**, hydrogen peroxide concentrations are plotted as a function of time (min).

DETAILED DESCRIPTION OF THE INVENTION

[0066] Referring to the drawings, like numerals indicate like elements and the same number appearing in more than one drawing refers to the same element. In addition, hereinafter, the following definitions apply:

[0067] "Sample" generally refers to a source of an analyte of interest. IMS methods and systems of the present invention are capable of detecting and analyzing peroxide provided in, or derived from, analytes in gas phase samples, liquid phase samples, solid phase samples and multiphase samples. Analysis provided by the present invention may involve direct sampling in the case of a sample having a gas phase component. Alternatively, analysis of samples may involve one or more sample preparation steps for generating a gas phase component, for example by sample heating or desorbing components of a sample to generate a gas phase sample having a peroxide component.

[0068] "Ion" refers generally to multiply or singly charged atoms, molecules, macromolecules having either positive or negative electric charge and to complexes, aggregates, clusters or fragments of atoms, molecules and macromolecules having either positive or negative electric charge.

[0069] "Analyte ion" or "detectable ion" refers to ions derived from analyte(s) of interest in a gas phase sample that are capable of separation on the basis of mobility under an applied electric field, and detected in the present IMS methods and systems so as to characterize the identity and/or concentration of the analyte(s) in the sample. The present methods and systems detect peroxide analytes by generation, characterization and detection of peroxide analyte ions.

[0070] "Dopant" refers to compounds that are added to an IMS analyzer to suppress formation of unwanted peaks detected by the IMS. A dopant can be capable of adjusting the drift times of ions. The dopants in the present invention may also be useful for facilitating charge transfer in the separation region and maintaining ion clusters as the clusters travel in the separation region. The IMS systems disclosed herein may be tuned to specifically suppress peaks associated with a variety of compounds. Dopants are useful in embodiments of the present invention for enhancing the sensitivity and selectivity of the present IMS analyzers for detecting, identifying and characterizing analytes in a gas sample. In some embodiments, dopants added to an IMS analyzer selectively adjust the composition and/or drift times of ions, for example, by shifting the drift times of ions such that they are different from the drift times of other ions generated in the analyzer (e.g., dopant ions, background ions/ions derived from impurities and interferants such as water vapor). In some embodiments, dopants added to an IMS analyzer selectively adjust the composition and/or drift times of background ions, for example by shifting the drift times of background ions such that they are different from the drift times of analyte ions. Use of dopants in this aspect of the present invention is useful for generating IMS spectra and detection conditions wherein peaks corresponding to detectable ions separated in the drift region do not significantly overlap with peaks corresponding to other ions generated in the analyzer such as background ions, dopant ions, ions derived from impurities and interferants such as water vapor. In certain embodiments, dopant in excess prevents formation of interfering or anomalous peaks. Dopants may be selected depending on the analyte to-be-detected. For example, the dopant may be selected to have a basicity that is between the basicity of the carrier gas and the analyte, for example. Examples of typical dopants include, but are not limited to, a substituted aryl compound or a substituted cyclic diene; wherein the substituted aryl compound or the substituted cyclic diene has at least one substituent selected from the group consisting of a hydroxyl group, a carbonyl group, an aldehyde group, an ester group, a carboxylic acid group and a carbonate ester group. Effective dopants for negative mode IMS detection of peroxide analytes include, but are not limited to, a substituted benzene derivative having at least one substituent selected from the group consisting of a hydroxyl group, a carbonyl group, an aldehyde group, an ester group, a carboxylic acid group and a carbonate ester group. In an embodiment of the present invention, the dopant is a substituted or unsubstituted phenol, or a substituted or unsubstituted quinone. In an embodiment wherein the formation and/or detection of potentially interfering ions, such as interfering ions originating from water vapor, is minimized the dopant provided to the IMS analyzer is methyl salicylate dopant and/or 2-hydroxyacetophenone.

[0071] "Dopant ions" refer to ions generated from ionization of one or more dopants provided to the ionization region of an IMS. As used herein, dopant ions expressly includes electrically charged monomers, dimers, clusters and complexes of dopants. As used herein, dopant expressly includes electrically charged fragments of dopants, dimers of dopants, trimers of dopants, clusters of dopants and fragments of dopant clusters. In some embodiments, dopant ions refer to negatively charged monomers, dimers, clusters, complexes and/or fragments of a dopant such as methyl salicylate. Dopants and dopants ions of the present invention interact with analyte(s) in a gas phase sample to generate ions that can be analyzed and detected so as to detect, identify and characterized the analyte(s) in the sample.

[0072] An ion may be a precursor ion or an intermediate ion that further reacts with other materials. Intermediate ion refers to ions formed from carrier gas(es) and drift gas(es) in an IMS analyzer. In some embodiments, intermediate ions participate in charge transfer reactions resulting in ionization of analytes, dopants or both analytes and dopants, thereby generating ions that are subsequently detected by an ion detector.

[0073] "Fluid communication" refers to the configuration of two or more elements such that a fluid (e.g., a gas or a liquid) is capable of transport, flowing and/or diffusing from one element to another element. Elements may be in fluid communication via one or more additional elements such as tubes, cells, containment structures, channels, valves, pumps or any combinations of these. In an embodiment, an ionization and separation region are said to be in fluid communication if at least a portion of dopant, drift gas and ions are capable of transiting from one region to the other. In certain aspects this fluid communication is one-way (e.g., drift gas traveling from the separation to the ionization region). The term fluid communication expressly encompasses device configurations wherein a fluid is capable of transport from a first region and/or device component to a second region and/or device component via diffusion through a membrane separating first and second regions and/or device components. In an embodiment, for example, an inlet is provided in fluid communication with an ionization region via a membrane, wherein analyte gas(es) diffuses through the membrane and thereby is transported from the inlet to the ionization region provided in fluid communication.

[0074] "Analyte" is used broadly to refer to detection of any substance of interest by IMS systems and methods, such as for emission, homeland security, contamination or process control measurements, for example. The present invention provides methods and system for the detection, identification and characterization of peroxide analytes.

[0075] "Carrier gas" refers to a gas that assists in transporting analyte, including analyte in a gas phase sample, to the ionization region. Carrier gas can range from a pure and inert gas such as nitrogen, or to a gas obtained from the environment surrounding the IMS, such as room air. The gas phase sample is optionally itself a room air carrier gas.

[0076] "Separation region" refers to the area of the IMS that separates ions based on the effective size of the ion (e.g., collisional cross-section). In an aspect, the separation region comprises a "drift region", such as a drift tube region wherein drift gas flows in a direction opposite to the E field-induced movement of the ions.

[0077] "Peroxide" and "peroxide analytes" are used synonymously and refer broadly to a class of compounds including hydrogen peroxide, hydroperoxides and organic peroxides. The present invention provides methods and systems for selectively detecting, identifying and characterizing peroxides, include but not limited to, hydrogen peroxide. Peroxides include, but are not limited to, peroxide-based explosives such as hexamethylenetriperoxidediamine (HMTD) and triacetone triperoxide (TATP).

[0078] Alkyl groups include straight-chain, branched and cyclic alkyl groups. Alkyl groups include those having from 1 to 30 carbon atoms. Alkyl groups include small alkyl groups having 1 to 3 carbon atoms. Alkyl groups include medium length alkyl groups having from 4-10 carbon atoms. Alkyl groups include long alkyl groups having more than 10 carbon atoms, particularly those having 10-30 carbon atoms. Cyclic alkyl groups include those having one or more rings. Cyclic alkyl groups include those having a 3-, 4-, 5-, 6-, 7-, 8-, 9- or 10-member carbon ring and particularly those having a 3-, 4-, 5-, 6-, or 7-member ring. The carbon rings in cyclic alkyl groups can also carry alkyl groups. Cyclic alkyl groups can include bicyclic and tricyclic alkyl groups. Alkyl groups are optionally substituted. Substituted alkyl groups include among others those which are substituted with aryl groups, which in turn can be optionally substituted. Specific alkyl groups include methyl, ethyl, n-propyl, iso-propyl, cyclopropyl, n-butyl, s-butyl, t-butyl, cyclobutyl, n-pentyl, branched-pentyl, cyclopentyl, n-hexyl, branched hexyl, and cyclohexyl groups, all of which are optionally substituted. Substituted alkyl groups include fully halogenated or semihalogenated alkyl groups, such as alkyl groups having one or more hydrogens replaced with one or more fluorine atoms, chlorine atoms, bromine atoms and/or iodine atoms. Substituted alkyl groups include fully fluorinated or semifluorinated alkyl groups, such as alkyl groups having one or more hydrogens replaced with one or more fluorine atoms. An alkoxyl group is an alkyl group linked to oxygen and can be represented by the formula R—O.

[0079] Alkenyl groups include straight-chain, branched and cyclic alkenyl groups. Alkenyl groups include those having 1, 2 or more double bonds and those in which two or more of the double bonds are conjugated double bonds. Alkenyl groups include those having from 2 to 20 carbon atoms. Alkenyl groups include small alkenyl groups having 2 to 3 carbon atoms. Alkenyl groups include medium length alkenyl groups having from 4-10 carbon atoms. Alkenyl groups include long alkenyl groups having more than 10 carbon atoms, particularly those having 10-20 carbon atoms. Cyclic alkenyl groups include those having one or more rings. Cyclic alkenyl groups include those in which a double bond is in the ring or in an alkenyl group attached to a ring. Cyclic alkenyl groups include those having a 3-, 4-, 5-, 6-, 7-, 8-, 9- or 10-member carbon ring and particularly those having a 3-, 4-, 5-, 6- or 7-member ring. The carbon rings in cyclic alkenyl groups can also carry alkyl groups. Cyclic alkenyl groups can include bicyclic and tricyclic alkyl groups. Alkenyl groups are optionally substituted. Substituted alkenyl groups include among others those which are substituted with alkyl or aryl groups, which groups in turn can be optionally substituted. Specific alkenyl groups include ethenyl, prop-1-enyl, prop-2-enyl, cycloprop-1-enyl, but-1-enyl, but-2-enyl, cyclobut-1-enyl, cyclobut-2-enyl, pent-1-enyl, pent-2-enyl, branched pentenyl, cyclopent-1-enyl, hex-1-enyl, branched hexenyl, cyclohexenyl, all of which are optionally substituted. Substituted alkenyl groups include fully halogenated or semihalogenated alkenyl groups, such as alkenyl groups having one or more hydrogens replaced with one or more fluorine atoms, chlorine atoms, bromine atoms and/or iodine atoms. Substituted alkenyl groups include fully fluorinated or semifluorinated alkenyl groups, such as alkenyl groups having one or more hydrogens replaced with one or more fluorine atoms.

[0080] Aryl groups include groups having one or more 5- or 6-member aromatic or heteroaromatic rings. Aryl groups can contain one or more fused aromatic rings. Heteroaromatic rings can include one or more N, O, or S atoms in the ring. Heteroaromatic rings can include those with one, two or three N, those with one or two O, and those with one or two S, or combinations of one or two or three N, O or S. Aryl groups are optionally substituted. Substituted aryl groups include among others those which are substituted with alkyl or alkenyl groups, which groups in turn can be optionally substituted. Specific aryl groups include phenyl groups, biphenyl groups, pyridinyl groups, and naphthyl groups, all of which are optionally substituted. Substituted aryl groups include fully halogenated or semihalogenated aryl groups, such as aryl groups having one or more hydrogens replaced with one or more fluorine atoms, chlorine atoms, bromine atoms and/or iodine atoms. Substituted aryl groups include fully fluori-

nated or semifluorinated aryl groups, such as aryl groups having one or more hydrogens replaced with one or more fluorine atoms.

[0081] Arylalkyl groups are alkyl groups substituted with one or more aryl groups wherein the alkyl groups optionally carry additional substituents and the aryl groups are optionally substituted. Specific alkylaryl groups are phenyl-substituted alkyl groups, e.g., phenylmethyl groups. Alkylaryl groups are alternatively described as aryl groups substituted with one or more alkyl groups wherein the alkyl groups optionally carry additional substituents and the aryl groups are optionally substituted. Specific alkylaryl groups are alkyl-substituted phenyl groups such as methylphenyl. Substituted arylalkyl groups include fully halogenated or semihalogenated arylalkyl groups, such as arylalkyl groups having one or more alkyl and/or aryl having one or more hydrogens replaced with one or more fluorine atoms, chlorine atoms, bromine atoms and/or iodine atoms.

[0082] Optional substitution of any alkyl, alkenyl and aryl groups includes substitution with one or more of the following substituents: halogens, —CN, —COOR, —OR, —COR, —OCOOR, —$CON(R)_2$, —$OCON(R)_2$, —$N(R)_2$, —NO_2, —SR, —SO_2R, —$SO_2N(R)_2$ or —SOR groups. Optional substitution of alkyl groups includes substitution with one or more alkenyl groups, aryl groups or both, wherein the alkenyl groups or aryl groups are optionally substituted. Optional substitution of alkenyl groups includes substitution with one or more alkyl groups, aryl groups, or both, wherein the alkyl groups or aryl groups are optionally substituted. Optional substitution of aryl groups includes substitution of the aryl ring with one or more alkyl groups, alkenyl groups, or both, wherein the alkyl groups or alkenyl groups are optionally substituted.

[0083] Optional substituents for alkyl, alkenyl and aryl groups include among others:

[0084] —COOR where R is a hydrogen or an alkyl group or an aryl group and more specifically where R is methyl, ethyl, propyl, butyl, or phenyl groups all of which are optionally substituted;

[0085] —COR where R is a hydrogen, or an alkyl group or an aryl groups and more specifically where R is methyl, ethyl, propyl, butyl, or phenyl groups all of which groups are optionally substituted;

[0086] —$CON(R)_2$ where each R, independently of each other R, is a hydrogen or an alkyl group or an aryl group and more specifically where R is methyl, ethyl, propyl, butyl, or phenyl groups all of which groups are optionally substituted; R and R can form a ring which may contain one or more double bonds;

[0087] —$OCON(R)_2$ where each R, independently of each other R, is a hydrogen or an alkyl group or an aryl group and more specifically where R is methyl, ethyl, propyl, butyl, or phenyl groups all of which groups are optionally substituted; R and R can form a ring which may contain one or more double bonds;

[0088] —$N(R)_2$ where each R, independently of each other R, is a hydrogen, or an alkyl group, acyl group or an aryl group and more specifically where R is methyl, ethyl, propyl, butyl, or phenyl or acetyl groups all of which are optionally substituted; or R and R can form a ring which may contain one or more double bonds.

[0089] —SR, —SO_2R, or —SOR where R is an alkyl group or an aryl groups and more specifically where R is methyl, ethyl, propyl, butyl, phenyl groups all of which are optionally substituted; for —SR, R can be hydrogen;

[0090] —OCOOR where R is an alkyl group or an aryl groups;

[0091] —$SO_2N(R)_2$ where R is a hydrogen, an alkyl group, or an aryl group and R and R can form a ring;

[0092] —OR where R═H, alkyl, aryl, or acyl; for example, R can be an acyl yielding —OCOR* where R* is a hydrogen or an alkyl group or an aryl group and more specifically where R* is methyl, ethyl, propyl, butyl, or phenyl groups all of which groups are optionally substituted;

[0093] Specific substituted alkyl groups include haloalkyl groups, particularly trihalomethyl groups and specifically trifluoromethyl groups. Specific substituted aryl groups include mono-, di-, tri, tetra- and pentahalo-substituted phenyl groups; mono-, di-, tri-, tetra-, penta-, hexa-, and hepta-halo-substituted naphthalene groups; 3- or 4-halo-substituted phenyl groups, 3- or 4-alkyl-substituted phenyl groups, 3- or 4-alkoxy-substituted phenyl groups, 3- or 4-RCO-substituted phenyl, 5- or 6-halo-substituted naphthalene groups. More specifically, substituted aryl groups include acetylphenyl groups, particularly 4-acetylphenyl groups; fluorophenyl groups, particularly 3-fluorophenyl and 4-fluorophenyl groups; chlorophenyl groups, particularly 3-chlorophenyl and 4-chlorophenyl groups; methylphenyl groups, particularly 4-methylphenyl groups, and methoxyphenyl groups, particularly 4-methoxyphenyl groups.

[0094] As to any of the above groups which contain one or more substituents, it is understood, that such groups do not contain any substitution or substitution patterns which are sterically impractical and/or synthetically non-feasible. In addition, the compounds of this invention include all stereochemical isomers arising from the substitution of these compounds.

[0095] FIG. **1**A provides a schematic diagram illustrating an ion mobility spectrometry analyzer **100** of the present invention useful for detecting, identifying and/or characterizing (e.g., measuring the concentration of) peroxides, such as hydrogen peroxide, in samples. As shown in FIG. **1**A, IMS analyzer **100** comprises hydrophobic membrane **110**, ionization region **130**, source of dopant **120**, separation region **160** and ion detector **180**. These elements of the present analyzer are provided in fluid communication with each other such that peroxide analytes in a sample are introduced to IMS analyzer **100** via hydrophobic membrane **110**, and undergo ionization in the ionization region **130**, so as to generate analyte ions that are subsequently separated in the separation region **160** on the basis of mobility and detected via ion detector **180**. In an alternative embodiment, an inlet is provided in fluid communication with ionization region **130**, source of dopant **120**, separation region **160** and/or ion detector **180** that does not have a hydrophobic membrane.

[0096] Referring again to FIG. **1**A, a flow of sample containing one or more peroxides (schematically shown by arrows **122**) is provided in contact with external surface **111** of hydrophobic membrane **110**. The flow of sample in this aspect of the present invention can be generated by any means known in the art of gas phase sampling including pumping gas from a monitoring environment or static sample through a tube, channel or other fluid containment region past the external surface **111** of hydrophobic membrane **110**. Use of chemically inert materials, such as Teflon® and glass, is useful for handling the samples prior to analysis and detection

for avoiding unwanted losses of peroxides during sample introduction. In some embodiments, the flow of sample containing one or more peroxides is contacted with the membrane at pressures near (e.g., within 20%) of atmospheric pressure. The composition and thickness of the hydrophobic membrane **110** is selected such that peroxides in the sample diffuse through the membrane and are, thereby, introduced into the IMS analyzer for detection and analysis. In this way, hydrophobic membrane **110** functions as an inlet in IMS analyzer **100**. The composition and thickness of hydrophobic membrane **110** is also selected such that transport of water vapor in the sample into the IMS analyzer is at least partially prevented. In this way, hydrophobic membrane **110** also functions to purify gas introduced to IMS analyzer **100** by reducing the water vapor component of the sample that is provided to the analyzer.

[0097] Referring again to FIG. **1**A, source of dopant **120** is provided in fluid communication with ionization region **130**, and is capable of introducing dopants into the ionization region **130** of IMS analyzer **100**. In some embodiments, source of dopant **120** provides a substituted phenol dopant, such as methyl salicylate or 2-hydroxyacetophenone, to the IMS analyzer **100**. Alternatively, source of dopant **120** may provide a substituted or unsubstituted quinone to the IMS analyzer **100**. Useful sources of dopants include permeation tube sources and molecular sieve sources. In an embodiment, the source of dopant is a polyethylene tube containing methyl salicylate dopant. Optionally a source of carrier gas(es) is provided so as to facilitate transport of dopant to the ionization region **130**. In the embodiment shown in FIG. **1**A, a flow of dopant and carrier gas (schematically shown as arrows **123**) is provided that that contacts internal surface **112** of hydrophobic membrane **110**. In this embodiment, the flow of dopant and carrier gas functions to "sweep" the internal surface **112** of the membrane so as to facilitate transport of peroxides diffusing through the membrane through the IMS analyzer. Useful carrier gases in the present invention include air and purified air. As will be understood by those having skill in the art, however, a wide range of other carrier gases (e.g., N_2, O_2, CO_2, Ar, etc.) can be employed in the present IMS methods and systems.

[0098] The mixture of peroxides, dopant and carrier gas is transported into ionization region **130** having ionization source **140** capable of generating ionizing radiation. Ionization sources useful in the present invention include radioactive sources, electrostatic sources (e.g., corona discharge) and photoionization sources. In an embodiment, ionization source **140** is a β particle source, such as a Ni^{63} radioactive source. Ionizing radiation generated by ionization source **140** interacts with peroxides, dopants, carrier gases and/or drift gases in the ionization region, thereby generating ions, including analyte ions, dopant ions and/or reagent ions. In some embodiments, negatively charged peroxide analyte ions are generated via direct ionization and/or ion-molecule reactions and/or ion-ion reactions in the ionization region involving peroxides, and optionally dopant and/or dopant ions

[0099] Referring again to FIG. **1**A, ion optics **150** is provided between ionization region **130** and separation region **160** for introducing ions into separation region **160**, for example via pulsed ion extraction. In an embodiment, the ion optics **150** comprise injection shutter or grid capable of injecting ions, including analyte ions and dopant ions, from the ionization region **130** into the separation region **160**. In an embodiment, IMS analyzer **100** operates in either normal mode or enhanced mode, as provided in U.S. Pat. No. 4,950,893 (where the function of the injection shutter or grid is reversed by having the shutter or grid normally biased open, with short pulses where the grid or shutter is closed). In the embodiment shown in FIG. **1**A, separation region **160** comprises a drift tube, optionally held at or near atmospheric pressure and/or at a constant temperature. Drift tube has inlets **170** for conducting a flow of drift gas (schematically illustrated as arrows **126**) through the drift tube. Ions (schematically illustrated as dotted arrows **125**), including analyte ions and dopant ions, are introduced to the separation region **160**. As shown in the Figure, drift gas is flown in a direction opposite to that of the ions passing through the drift tube. An electric potential is applied to ions in the drift tube so they undergo acceleration and separation on the basis of ion mobility. Specifically, separation in the drift tube separates analyte ions from other ions, such as dopant ions and background ions generated in the ionization region. In an embodiment, drift gas comprises dopant, such that dopant is provided to the ionization region via drift gas flow **126**.

[0100] Ion detector **180** is provided at the end of separation region **160** so as to receive and detect ions that have been separated on the basis of mobility. Useful ion detectors in the present invention include, but are not limited to a Faraday cup or a microchannel plate detector. In some embodiments, detector **180** is gated at preselected times so as to selectively detect analyte ions and/or dopants ions having drift times that are different than the drift times of other ions generated in the analyzer. Alternatively, detector **180** may be configured to detect ions continuously as a function of drift time so as to generate an IMS spectrum having peaks corresponding to ions exhibiting different drift times.

[0101] FIG. **1**B provides a schematic diagram illustrating an alternative IMS analyzer configuration of the present invention. As shown in FIG. **1**B, the inlet system for introducing the sample differs from that shown in FIG. **1**A. In the configuration shown in FIG. **1**B, peroxides are transported through hydrophobic membrane **110**, are mixed with dopant and carrier gas, and are subsequently transported directly past ionization source **140** wherein they undergo ionization and form analyte ions. As shown in FIG. **1**B, the fluid path of exhaust gas is also configured differently in this analyzer. In an alternative embodiment, an inlet is provided in fluid communication with ionization region **130**, source of dopant **120**, separation region **160** and/or ion detector **180** that does not have a hydrophobic membrane.

[0102] FIG. **1**C is a schematic of an alternative IMS analyzer, wherein the inlet system corresponds to the exhaust port depicted in FIG. **1**B and the exhaust port is positioned similar to the exhaust port of FIG. **1**A. The inlet port is optionally a threaded recess that connects a ⅛" outer diameter PFA tubing to deliver the sample to the IMS. The pressure differential between the inside of the IMS cell and the ambient pressure is typically between about 3 to 4 torr. In addition, the system in FIG. **1**C does not have a hydrophobic membrane or a carrier flow input separate from the air sample. Flow controller **230**, such as a flow controller **230** that is positioned at the exhaust outlet, provides a selectable ambient air sample **122** inflow rate or linear velocity that can be tailored to a specific operating condition.

[0103] Optionally, analyzer **100** of the present invention further comprises a calibration system or calibration verification system having source of calibration gas **200** in fluid communication with ionization region **130**. Source of cali-

bration gas **200** is provided such that one or more calibration gas can be provided to the ionization region **130** in preselected amounts, at preselected concentrations and/or at preselected rates. In an embodiment useful for detection and characterization of hydrogen peroxide, the source of calibration gas is a source of acetic acid, such as an acetic acid permeation tube source capable of emitting acetic acid at a know constant rate or a plurality of known constant rates. Use of acetic acid as a calibration gas is particularly useful because it generates a calibration ion(s) having a similar drift time to that of hydrogen peroxide analyte ions. In addition, acetic acid is a stable and nontoxic compound. The calibration system may optional further comprise a temperature control system operationally connected to the source of calibration gas **200** that is capable of controlling the temperature of the source of calibration gas, for example to provide source of calibration gas **200** held at a constant temperature. Use of a temperature control system is useful for controlling the rate of emission of calibration gas into the ionization region and/the concentration of calibration gas in the ionization region. Calibration gas in the ionization region generates calibration ions which are provided to the separation region, undergo separation on the basis of mobility and are detected. By measuring the signal and/or drift time corresponding to a known concentration/amount of calibration gas, the sensitivity, signal response characteristics and/or resolution can be analyzed so as to verify the calibration of an IMS analyzer of the present invention or to re-calibrate if necessary.

EXAMPLE 1

Vaporous Hydrogen Peroxide Measurements Using Ion Mobility Spectrometry

Background

[0104] To assess the capability of systems and methods for sensing of peroxide compounds in gas samples, an IMS analyzer of the present invention employing a hydrophobic membrane inlet system and a methyl salicylate dopant was used to detect and quantify the concentration of gas phase hydrogen peroxide. Gas phase standards comprising known hydrogen peroxide concentrations were prepared and used to assess the capabilities of the present IMS methods and systems for detecting hydrogen peroxide. In addition, measurements of hydrogen peroxide concentrations during aseptic processing were also carried out using the present IMS analyzers and methods. The results provided herein demonstrate the systems and methods of the present invention provide sensitive and selective detection of hydrogen peroxide under a range of operating conditions and sample environments.

[0105] The advent of aseptic manufacturing technology has led to an increase in the adoption of controlled clean devices for the assurance of sterility. To sterilize these environments between batches and to ensure that cross contamination does not occur, Vaporized Hydrogen Peroxide (VHP) is commonly used. The measurement of the VHP in these environments is required for proof of two functions; a higher level for sterilization and a lower limit to establish a purged environment. Currently two different instruments, utilizing two different monitoring techniques, are required to perform complete certification of the process, increasing initial and on-going cost-of-ownership. The hydrogen peroxide IMS analyzer of the present invention, in contrast, employs a single instrument with a dual detection range; this enables an accurate measurement of VHP at both high and low concentrations using a single monitoring technique.

[0106] In the present example, experimental performance testing compares measurements of VHP in a two-glove isolator using a Hydrogen Peroxide IMS analyzer of the present invention with side-by-side data obtained from a near infrared hydrogen peroxide monitor (NIR) and an electrochemical hydrogen peroxide monitor (E Chem. Cell).

Description of Monitoring Technology

[0107] The present hydrogen peroxide IMS analyzer utilizes ion mobility spectrometry (IMS) to detect and monitor hydrogen peroxide with high sensitivity and selectivity. As discussed herein, IMS is an ionization-based time of flight technique, performed at atmospheric pressure. The air sample is pulled through a Teflon® diaphragm pump and drawn over a semipermeable hydrophobic membrane by way of an internal eductor. The membrane serves several purposes in this analyzer configuration. It protects the interior of the IMS cell from particles and high moisture levels, provides a degree of selectivity, and allows various levels of sensitivity based on permeation rate. The molecules of interest, such as hydrogen peroxide, permeate through the membrane, are mixed with dopant reagent molecules, and are delivered to the ionization region of the cell, which contains a small Ni^{63} beta emitter. There, the sample is ionized as a result of a series of ion-molecule reactions. The dopant reagent molecules enter into the ion-molecule chain of reactions to provide a degree of selectivity based on the charge affinity of the analyte. In some analyzers of the present invention particularly useful for detecting hydrogen peroxide, the dopant is substituted phenol, such as methyl salicylate.

[0108] Once the sample is ionized, the ions begin to drift toward the opposite end of the cell due to the influence of an electric field. A shutter grid is located in the tube, which can be biased electrically to either block the ions or allow them to pass through. This shutter grid is pulsed periodically to allow ions to enter the separation region. There, the ions begin to separate out based on their size and shape while drifting counter to an inert gas flow introduced at the detector end of the tube. A collector plate located at the end of the tube detects the arrival of the ions by producing a current. This current is amplified to produce a time of flight spectrum.

[0109] FIG. **2** provides an IMS time of flight spectrum for the detection of hydrogen peroxide obtained using the present IMS analyzer with a methyl salicylate dopant. Ions are identified by their characteristic drift time position in the spectrum as seen in FIG. **2**. As shown in FIG. **2**, two primary peaks are observed in the IMS spectrum: (i) a first peak at lower times (approx. 105) corresponding to analyte ions, and (ii) a second peak at higher times (approx. 145) corresponding to dopant ions. The analyte ion peak provides a unique signature for identifying peroxide analytes that quantitatively correlates with peroxide concentration in a sample. A small shoulder is observable on the analyte ion peak, which may be attributable to ions generated from water vapor.

[0110] FIG. **3** provides an overlap plot corresponding to a plurality of measurements of the IMS spectrum for peroxide detection under the same sample and analyzer conditions. The spectra shown in FIG. **3** indicate that the present IMS analyzer provides very reproducible spectra. For example, the IMS spectra shown in FIG. **3** show a constant peak height

ratio equal to approximately 0.1. Peak height ratio is defined in these measurements is define by the following expression:

$$IMS\ \text{Response} = \left(\frac{H_{analyte}}{H_{analyte} + H_{dopant}} \right)$$

[0111] wherein $H_{analyte}$ is the peak height of the analyte ion peak and H_{dopant} is the peak height of the dopant ion peak. FIG. **4** provides a plot of hydrogen peroxide concentration versus IMS response in terms of observed peak height ratio.

[0112] FIG. **5** provides a plot of instrument response expressed in units of hydrogen peroxide concentration verse time for the introduction of a 10 ppm sample of hydrogen peroxide. In these experiments a known amount of hydrogen peroxide is provided to the analyzer at a constant rate. At some time after introduction of the hydrogen peroxide sample, the source is shut off to characterize the cleardown performance of the instrument. As shown in this plot, the present IMS analyzer provides very fast response times (on the order of seconds) and good cleardown performance for experimental conditions of hydrogen peroxide concentrations in the 10s of ppm range.

[0113] FIG. **6** provides a plot of instrument response expressed in units of hydrogen peroxide concentration verse time (min) for the introduction of a 600 ppm sample of hydrogen peroxide. In these experiments a known amount of hydrogen peroxide was provided to the analyzer at a constant rate. At some time after introduction of the hydrogen peroxide sample, the source was shut off using a dilution switch (100 to 1 dilution conditions) to characterize the cleardown performance of the instrument. As shown in this plot, the present IMS analyzer provides very fast response times (on the order of a few minutes) and good cleardown performance for experimental conditions of hydrogen peroxide concentrations in the 100s of ppm range.

[0114] FIG. **7** shows the experimental results for a stability test of the present IMS analyzer. Peroxide concentration is plotted verses time (min) in FIG. **7**. In these experiments 5 ppm of acetic acid was introduced into the IMS analyzer, and the IMS signal was measured over a time domain corresponding to a 24 hour period. Acetic acid was used in these experiments because it exhibits a very similar drift time as that of hydrogen peroxide. A permeation tube source was used to provide the acetic acid to the IMS analyzer at a known and very stable rate. The data in FIG. **7** also demonstrate that the present IMS analyzer is capable of very stable and reproducible operation.

[0115] Table 1 provides a summary of device and performance specifications for a IMS analyzer of the present invention.

TABLE 1

Summary of device and performance specifications for a IMS analyzer of the present invention

Analyzer Specifications	
Range	0-20 ppm; 20-2000 ppm (using a 100:1 internal dilution module)
Detection Limit	0.030 ppm
On-Board Calibration	10 ppm span calibration with acetic acid surrogate
Response and Clear Down	Typical curves shown in FIGS. 6 (no dilution) and 7 (with dilution)

TABLE 1-continued

Summary of device and performance specifications for a IMS analyzer of the present invention

Analyzer Specifications	
Dimensions	Wall-mounted analyzer, 20 × 20 × 9 in
Weight	50 lbs.
Operating Ambient Temp.	−40° F.-122° F.
Outputs	Local digital display, 4-20 mA loop, 2 alarm relay, 1 fault relay, RS-232, and Ethernet
Sample Requirements	Sample in the vapor phase and delivered to the analyzer at atmospheric pressure at a minimum of 800 mL/min
Maintenance Schedule	10 minute operation every 6 months
Power Supply	115 VAC, 50/60 Hz
Current Consumption	5 amps
Instrument Air Supply	−40° F. dew point, oil-free, 10 L/min required

Test Conditions

[0116] The VHP generator was connected to a 22 ft^3 two-glove isolator. Inside the isolator, two fans provided mixing circulation. Approximately 12 ft of ¼" diameter Teflon® (PFA) tubing was used to transfer the sample from the isolator to the IMS analyzer. The Teflon® tubing entered the isolator through one of the glove fingertips that was cut open. The tube was sealed to the glove using parafilm and was located in the middle of the isolator, immediately above the near infrared monitor's optical path and adjacent to the electrochemical cell. IMS analyzer exhaust was transferred from the analyzer to the isolator via 12 ft of 1" diameter tubing that connected directly to a port on the side of the isolator.

[0117] The near infrared optical bench was installed on the bottom of the isolator and the fiber optic cables were fed out a port on the side of the isolator. The electrochemical cell was installed in a cut glove finger.

[0118] Data collection for the IMS analyzer and the electrochemical cell was performed using software to log the 4-20 mA outputs and convert the output to ppm concentration values. The near infrared monitor output was logged by RS-232 serial communications with HyperTerminal®. The output of the near infrared monitor was converted to ppm in Excel after the testing was completed (multiply by a conversion factor of 712).

Dehumidification Air Flow:	20 cfm	Dehumidify to:	2.3 mg/l
		Dehumidification Time:	10 min
Conditioning Air Flow:	20 cfm	Condition Injection Rate:	4.2 g/min
		Condition Time:	2 min
Sterilization Air Flow:	16 cfm	Sterilize Injection Rate:	1.8 g/min
		Sterilization Time:	1 hour
Aerate Air Flow:	20 cfm	Aerate Time:	2 hours
Vaporizer Set Temp:	212° F.	Chamber Pressure Set:	0.20"
Preheater Set Temp:	194° F.	High Pressure Alarm:	0.80"
		Low Pressure Alarm:	0.00"

Results

[0119] To evaluate the sensitivity of the IMS analyzer, the noise was measured while monitoring a "zero gas" stream that is generated within the analyzer. FIG. **8** provides a plot of

the signal-to-noise ratio as a function of time for an IMS analyzer of the present invention for conditions of no hydrogen peroxide gas phase gas analyte, i.e. zero gas stream. The standard deviation of the noise is roughly 0.010 ppm. This value is comparable to observations made in the calibration laboratory prior to shipping. The limit of detection is typically given as 3* standard deviation of the noise, in this case 0.030 ppm.

[0120] To assess the response of the IMS analyzer, a span calibration check was performed using the analyzer's on-board calibration system. The span calibration system uses acetic acid as a surrogate calibration gas. FIG. **9** provides experimental results corresponding to a typical span calibration check cycle. As shown in FIG. **9** the IMS signal response of the present IMS analyzer is very stable.

[0121] The IMS analyzer was compared to the NIR monitor during sterilization cycles. The results compare very well at the higher concentrations. The NIR monitor was recently calibrated. It has a published sensitivity level of 71 ppm, so its data is not expected to match at the lower concentration levels. FIG. **10** provides a comparison plot showing experimental data for the present IMS analyzer, electrochemical cell and NIR monitor for the high hydrogen peroxide conditions of the sterilization phase. In this test and in some later tests, it appears that the NIR monitor output may be drifting over time scales of hours. It is interesting to note that after about 1 hour of aeration, there is still 6 ppm of hydrogen peroxide in the isolator.

[0122] After seeing the hydrogen peroxide concentrations decrease slowly during aeration, a test was conducted to determine if this slow concentration decrease was due to outgassing peroxide from the IMS sample inlet tubing. A sterilization cycle was performed and aeration continued until the concentration inside the isolator was reduced to around 7 ppm. Then, the sample inlet tube was cut at the isolator, leaving the end of the long inlet tube exposed to ambient air immediately adjacent to the isolator. FIG. **11** provides a plot of IMS signal (in units of peroxide concentration) as a function of time for experimental conditions wherein the inlet tube was cut at the isolator. As shown in FIG. **11**, the measured peroxide concentration dropped to less than 1 ppm within one or two minutes, demonstrating that the sample inlet tubing was not affecting the isolator clear down measurements.

[0123] It is interesting to note that the hydrogen peroxide concentration immediately adjacent (<<1" away) to the exterior of the isolator was measured at 200-250 ppb, while the concentration several feet away from the isolator was measured at 70 ppb.

[0124] FIG. **12** provides experimental results comparing the NIR monitor, an electrochemical monitor, and the present IMS analyzer for monitoring hydrogen peroxide during conditioning, sterilization and aeration phases. This test is similar to FIG. **10** in that there is a good correlation between the IMS data and NIR data at high concentrations, but evidence reflects that the NIR monitor output drifted slightly during the test period. The electrochemical cell data matches fairly well with the IMS data at low concentrations, but reads 30-40% higher than the IMS and NIR at sterilization concentrations.

[0125] FIG. **13** provides an expanded view of the experimental data shown in FIG. **12** corresponding to the aeration cycle. FIG. **14** provides a comparison of hydrogen peroxide concentrations measured by the present IMS analyzer and the electrochemical cell during the aeration phase. At low concentrations, the NIR monitor does not match well with the electrochemical or IMS monitors. As mentioned before, this is expected due to the detection limit. This particular electrochemical monitor matches fairly well with the IMS until the concentration reduces to around 9 ppm then it bounces between zero, 5 ppm, and 10 ppm. When the concentration is below 8 or 9 ppm, the electrochemical cell output was zero. In FIG. **14**, the aeration was turned off at 14:00. With the isolator closed (circulation fans on), outgassing peroxide increase the concentration in the isolator from 6.5 ppm to 10.0 ppm in 10 minutes. When the concentration increased above 8 or 9 ppm, the electrochemical cell resumed non-zero measurements that match well with the IMS data.

[0126] FIG. **15** provides a plot of hydrogen peroxide concentrations determined using the present IMS peroxide analyzer for filing isolator conditioning and sterilization. In FIG. **15**, hydrogen peroxide concentrations are plotted as a function of time (min).

[0127] FIG. **16** provides a plot of hydrogen peroxide concentrations determined using the present IMS peroxide analyzer for monitoring transfer isolator during conditioning, sterilization, and aeration. In FIG. **16**, hydrogen peroxide concentrations are plotted as a function of time (min).

[0128] FIG. **17** provides a plot of hydrogen peroxide concentrations determined using the present IMS peroxide analyzer for monitoring completion of aeration cycle on transfer isolator. In FIG. **17**, hydrogen peroxide concentrations are plotted as a function of time (min).

CONCLUSIONS

[0129] The present hydrogen peroxide IMS analyzer has the ability to measure high concentrations during the sterilization cycle and the sensitivity to accurately monitor completion of the aeration purge cycle. IMS systems and methods of the present invention enable continuous monitoring and documentation of production isolator sterilization cycles.

STATEMENTS REGARDING INCORPORATION BY REFERENCE AND VARIATIONS

[0130] U.S. Provisional applications 60/952,669 filed Jul. 30, 2007 is hereby incorporated by reference in their entireties to the extent not inconsistent with the present description. All references throughout this application, for example patent documents including issued or granted patents or equivalents; patent application publications; and non-patent literature documents or other source material; are hereby incorporated by reference herein in their entireties, as though individually incorporated by reference, to the extent each reference is at least partially not inconsistent with the disclosure in this application (for example, a reference that is partially inconsistent is incorporated by reference except for the partially inconsistent portion of the reference).

[0131] The terms and expressions which have been employed herein are used as terms of description and not of limitation, and there is no intention in the use of such terms and expressions of excluding any equivalents of the features shown and described or portions thereof, but it is recognized that various modifications are possible within the scope of the invention claimed. Thus, it should be understood that although the present invention has been specifically disclosed by preferred embodiments, exemplary embodiments and optional features, modification and variation of the concepts

herein disclosed may be resorted to by those skilled in the art, and that such modifications and variations are considered to be within the scope of this invention as defined by the appended claims. The specific embodiments provided herein are examples of useful embodiments of the present invention and it will be apparent to one skilled in the art that the present invention may be carried out using a large number of variations of the devices, device components, methods steps set forth in the present description. As will be obvious to one of skill in the art, methods and devices useful for the present methods can include a large number of optional composition and processing elements and steps.

[0132] When a group of substituents is disclosed herein, it is understood that all individual members of that group and all subgroups. When a Markush group or other grouping is used herein, all individual members of the group and all combinations and subcombinations possible of the group are intended to be individually included in the disclosure.

[0133] Every formulation or combination of components described or exemplified herein can be used to practice the invention, unless otherwise stated.

[0134] Whenever a range is given in the specification, for example, a temperature range, a time range, or a composition or concentration range, all intermediate ranges and subranges, as well as all individual values included in the ranges given are intended to be included in the disclosure. It will be understood that any subranges or individual values in a range or subrange that are included in the description herein can be excluded from the claims herein.

[0135] All patents and publications mentioned in the specification are indicative of the levels of skill of those skilled in the art to which the invention pertains. References cited herein are incorporated by reference herein in their entirety to indicate the state of the art as of their publication or filing date and it is intended that this information can be employed herein, if needed, to exclude specific embodiments that are in the prior art. For example, when composition of matter are claimed, it should be understood that compounds known and available in the art prior to Applicant's invention, including compounds for which an enabling disclosure is provided in the references cited herein, are not intended to be included in the composition of matter claims herein.

[0136] As used herein, "comprising" is synonymous with "including," "containing," or "characterized by," and is inclusive or open-ended and does not exclude additional, unrecited elements or method steps. As used herein, "consisting of" excludes any element, step, or ingredient not specified in the claim element. As used herein, "consisting essentially of" does not exclude materials or steps that do not materially affect the basic and novel characteristics of the claim. In each instance herein any of the terms "comprising", "consisting essentially of" and "consisting of" may be replaced with either of the other two terms. The invention illustratively described herein suitably may be practiced in the absence of any element or elements, limitation or limitations which is not specifically disclosed herein.

[0137] One of ordinary skill in the art will appreciate that starting materials, biological materials, reagents, synthetic methods, purification methods, analytical methods, assay methods, and biological methods other than those specifically exemplified can be employed in the practice of the invention without resort to undue experimentation. All art-known functional equivalents, of any such materials and methods are intended to be included in this invention. The terms and expressions which have been employed are used as terms of description and not of limitation, and there is no intention that in the use of such terms and expressions of excluding any equivalents of the features shown and described or portions thereof, but it is recognized that various modifications are possible within the scope of the invention claimed. Thus, it should be understood that although the present invention has been specifically disclosed by preferred embodiments and optional features, modification and variation of the concepts herein disclosed may be resorted to by those skilled in the art, and that such modifications and variations are considered to be within the scope of this invention as defined by the appended claims.

We claim:

1. An ion mobility spectrometry analyzer for detecting peroxide analytes in a sample; said analyzer comprising:

an inlet for introducing said peroxide analytes into an ionization region of said analyzer;

a source of dopant for providing dopant to said analyzer, wherein said dopant is a substituted aryl compound or a substituted cyclic diene; wherein the substituted aryl compound or the substituted cyclic diene has at least one substituent selected from the group consisting of a hydroxyl group, a carbonyl group, an aldehyde group, an ester group, a carboxylic acid group and a carbonate ester group;

said ionization region provided in fluid communication with said inlet and said source of dopant for receiving said peroxide analytes and said dopant, said ionization region having an ionization source for generating analyte ions from said peroxide analytes;

a separation region in fluid communication with said ionization region for receiving and separating said analyte ions on the basis of ion mobility; and

a detector positioned in fluid communication with said separation region for receiving and detecting said analyte ions separated on the basis of ion mobility.

2. The analyzer of claim **1** wherein said inlet is a hydrophobic membrane that at least partially prevents transmission of water vapor in said sample into said ionization region of said analyzer.

3. The analyzer of claim **2** wherein said hydrophobic membrane is preferentially permeable to said peroxide analytes relative to water vapor.

4. The analyzer of claim **2** wherein said hydrophobic membrane is a coated membrane.

5. The analyzer of claim **4** wherein said hydrophobic membrane is a microporous membrane having a hydrophobic coating.

6. The analyzer of claim **5** wherein said hydrophobic coating is a silicone hydrophobic coating or a fluorocarbon hydrophobic coating.

7. The analyzer of claim **5** wherein said hydrophobic coating has a thickness selected from the range of 10 microns to 100 microns.

8. The analyzer of claim **5** wherein said microporous membrane is a Goretex membrane.

9. The analyzer of claim **2** wherein said hydrophobic membrane has a thickness selected from the range of 0.1 millimeter to 10 millimeters.

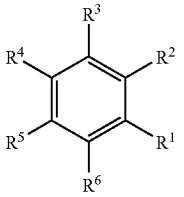
10. The analyzer of claim **2** wherein said hydrophobic membrane has a composition and thickness providing a concentration of water vapor in the analyzer less than or equal to 100 ppm.

11. The analyzer of claim **1** wherein said dopant is a substituted benzene derivative having at least one substituent selected from the group consisting of a hydroxyl group, a carbonyl group, an aldehyde group, an ester group, a carboxylic acid group and a carbonate ester group.

12. The analyzer of claim **1** wherein said dopant is a substituted or unsubstituted phenol, or a substituted or unsubstituted quinone.

13. The analyzer of claim **11** wherein said substituted benzene derivative has the formula:

(F1)

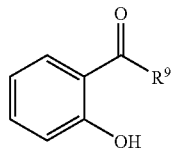


wherein each of R^1, R^2, R^3, R^4, R^5, and R^6, is independently selected from the group consisting of a hydrogen, a halogen, CN, OR, COOR, OCOOR, COR, $N(R)_2$, SR, SO_2R, SOR, a substituted or unsubstituted C_1-C_{20} alkyl group, a substituted or unsubstituted C_2-C_{20} alkenyl group, a substituted or unsubstituted C_2-C_{20} alkynyl group, a substituted or unsubstituted C_1-C_{20} alkoxy group, and a substituted or unsubstituted C_4-C_{20} aryl group; wherein each R, independent of any other R in any listed group, is selected from H, a substituted or unsubstituted C_1-C_{20} alkyl group, a substituted or unsubstituted C_4-C_{20} aryl group, a substituted or unsubstituted C_2-C_{20} alkenyl group, a substituted or unsubstituted C_2-C_{20} alkynyl group, and a substituted or unsubstituted C_3-C_{20} acyl group, and wherein at least one of R^1, R^2, R^3, R^4, R^5, and R^6 is a hydroxyl group, a carbonyl group, an aldehyde group, an ester group, a carboxylic acid group or a carbonate ester group.

14. The analyzer of claim **13** wherein said substituted benzene derivative is a phenol, wherein at least one of R^1, R^2, R^3, R^4, R^5, and R^6 is a hydroxyl group.

15. The analyzer of claim **1** wherein said dopant provided to the analyzer is a substituted phenol having the formula:

(F2)

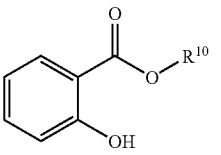


wherein R^9 is selected from the group consisting of a hydrogen, a halogen, CN, OR, COOR, OCOOR, COR, $N(R)_2$, SR, SO_2R, SOR, a substituted or unsubstituted C_1-C_{20} alkyl group, a substituted or unsubstituted C_2-C_{20} alkenyl group, a substituted or unsubstituted C_2-C_{20} alkynyl group, a substituted or unsubstituted C_1-C_{20} alkoxy group, and a substituted or unsubstituted C_4-C_{20} aryl group; and wherein each R, independent of any other R in any listed group, is selected from H, a substituted or unsubstituted C_1-C_{20} alkyl group, a substituted or unsubstituted C_4-C_{20} aryl group, a substituted or unsubstituted C_2-C_{20} alkenyl group, a substituted or unsubstituted C_2-C_{20} alkynyl group, and a substituted or unsubstituted C_3-C_{20} acyl group.

16. The analyzer of claim **15** wherein R^9 is a hydrogen or a C_1-C_{10} substituted or unsubstituted alkyl group.

17. The analyzer of claim **1** wherein said dopant provided to the analyzer is a substituted phenol having the formula:

(F3)



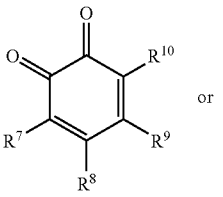
wherein R^{10} is selected from the group consisting of a hydrogen, a halogen, CN, OR, COOR, OCOOR, COR, $N(R)_2$, SR, SO_2R, SOR, a substituted or unsubstituted C_1-C_{20} alkyl group, a substituted or unsubstituted C_2-C_{20} alkenyl group, a substituted or unsubstituted C_2-C_{20} alkynyl group, a substituted or unsubstituted C_1-C_{20} alkoxy group, and a substituted or unsubstituted C_4-C_{20} aryl group; and wherein each R, independent of any other R in any listed group, is selected from H, a substituted or unsubstituted C_1-C_{20} alkyl group, a substituted or unsubstituted C_4-C_{20} aryl group, a substituted or unsubstituted C_2-C_{20} alkenyl group, a substituted or unsubstituted C_2-C_{20} alkynyl group, and a substituted or unsubstituted C_3-C_{20} acyl group.

18. The analyzer of claim **17** wherein R^{10} is a hydrogen or a C_1-C_{10} substituted or unsubstituted alkyl group.

19. The analyzer of claim **1** wherein said dopant provided to the analyzer is methyl salicylate or is 2-hydroxyacetophenone.

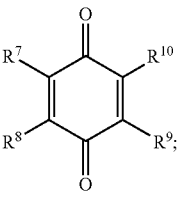
20. The analyzer of claim **1** wherein said dopant provided to the analyzer is a substituted or unsubstituted quinone having the formula:

(F6)



or

(F7)

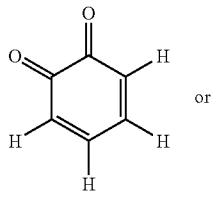


wherein each of R^7, R^8, R^9 and R^{10} is independently selected from the group consisting of: a hydrogen, a halogen, CN, OR, COOR, OCOOR, COR, $N(R)_2$, SR, SO_2R, SOR, a substituted or unsubstituted C_1-C_{20} alkyl group, a substituted or unsubstituted C_2-C_{20} alkenyl group, a substituted or unsubstituted C_2-C_{20} alkynyl group, a substituted or unsubstituted C_1-C_{20} alkoxy group, and a substituted or unsubstituted

C_4-C_{20} aryl group; and wherein each R, independent of any other R in any listed group, is selected from H, a substituted or unsubstituted C_1-C_{20} alkyl group, a substituted or unsubstituted C_4-C_{20} aryl group, a substituted or unsubstituted C_2-C_{20} alkenyl group, a substituted or unsubstituted C_2-C_{20} alkynyl group, and a substituted or unsubstituted C_3-C_{20} acyl group.

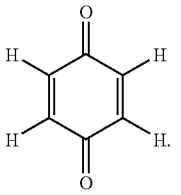
21. The analyzer of claim **1** wherein said dopant provided to the analyzer is a quinone having the formula:

(F8)



or

(F9)



22. The analyzer of claim **1** wherein said source of dopants generates a concentration of dopant in said ionization region selected from the range of 1 ppm to 100 ppm.

23. The analyzer of claim **1** wherein said source of dopant is a source of methyl salicylate, and wherein the source of methyl salicylate is a polyethylene tube containing liquid and gaseous methyl salicylate.

24. The analyzer of claim **1** further comprising an ion shutter or grid provided between said ionization region and said separation region for introducing said analyte ions into said separation region.

25. The analyzer of claim **1** further comprising a source of acetic acid in fluid communication with said ionization region for calibrating said ion mobility spectrometry analyzer or for verifying the calibration of said ion mobility spectrometry analyzer.

26. A method for selectively detecting one or more peroxide analytes in a sample; said method comprising:

providing an ion mobility spectrometry analyzer having an inlet, ionization region, separation region and detector;

passing at least a portion of said peroxide analytes through said inlet of said analyzer into said ionization region of said analyzer;

providing dopant to said ionization region, separation region or both of said analyzer, wherein said dopant is a substituted aryl compound or a substituted cyclic diene; wherein the substituted aryl compound or the substituted cyclic diene has at least one substituent selected from the group consisting of a hydroxyl group, a carbonyl group, an aldehyde group, an ester group, a carboxylic acid group and a carbonate ester group;

generating analyte ions from said peroxide analytes in said ionization region;

passing said analyte ions through said separation region of said ion mobility spectrometry analyzer, said separation region provided in fluid communication with said ionization source, wherein said analyte ions are separated on the basis of ion mobility; and

detecting said analyte ions separated on the basis of ion mobility using a detector provided in fluid communication with said separation region.

27. The method of claim **26** wherein said inlet is a hydrophobic membrane that at least partially prevents transmission of water vapor in said sample into said ionization region of said analyzer.

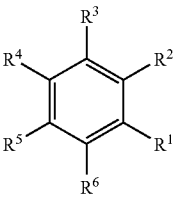
28. The method of claim **26** wherein said step of providing dopant to said ionization region suppresses interference from ions generated from water in said analyzer.

29. The method of claim **26** wherein said dopant is a substituted benzene derivative having at least one substituent selected from the group consisting of a hydroxyl group, a carbonyl group, an aldehyde group, an ester group, a carboxylic acid group and a carbonate ester group.

30. The method of claim **26** wherein said dopant is a substituted or unsubstituted phenol, or a substituted or unsubstituted quinone.

31. The method of claim **29** wherein said substituted benzene derivative has the formula:

(F1)

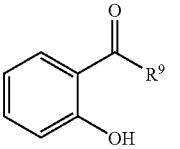


wherein each of R^1, R^2, R^3, R^4, R^5, and R^6, is independently selected from the group consisting of: a hydrogen, a halogen, CN, OR, COOR, OCOOR, COR, $N(R)_2$, SR, SO_2R, SOR, a substituted or unsubstituted C_1-C_{20} alkyl group, a substituted or unsubstituted C_2-C_{20} alkenyl group, a substituted or unsubstituted C_2-C_{20} alkynyl group, a substituted or unsubstituted C_1-C_{20} alkoxy group, and a substituted or unsubstituted C_4-C_{20} aryl group; wherein each R, independent of any other R in any listed group, is selected from H, a substituted or unsubstituted C_1-C_{20} alkyl group, a substituted or unsubstituted C_4-C_{20} aryl group, a substituted or unsubstituted C_2-C_{20} alkenyl group, a substituted or unsubstituted C_2-C_{20} alkynyl group, and a substituted or unsubstituted C_3-C_{20} acyl group, and wherein at least one of R^1, R^2, R^3, R^4, R^5, and R^6 is a hydroxyl group, a carbonyl group, an aldehyde group, an ester group, a carboxylic acid group or a carbonate ester group.

32. The method of claim **31** wherein said substituted benzene derivative is a phenol, and wherein at least one of R^1, R^2, R^3, R^4, R^5, and R^6 is a hydroxyl group.

33. The method of claim **26** wherein said dopant provided to the analyzer is a substituted phenol having the formula:

(F2)



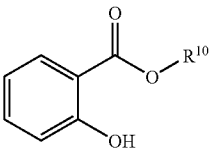
wherein R^9 is selected from the group consisting of a hydrogen, a halogen, CN, OR, COOR, OCOOR, COR, $N(R)_2$, SR, SO_2R, SOR, a substituted or unsubstituted C_1-C_{20} alkyl group, a substituted or unsubstituted C_2-C_{20} alkenyl group, a substituted or unsubstituted C_2-C_{20} alkynyl group, a substi-

tuted or unsubstituted C_1-C_{20} alkoxy group, and a substituted or unsubstituted C_4-C_{20} aryl group; and wherein each R, independent of any other R in any listed group, is selected from H, a substituted or unsubstituted C_1-C_{20} alkyl group, a substituted or unsubstituted C_4-C_{20} aryl group, a substituted or unsubstituted C_2-C_{20} alkenyl group, a substituted or unsubstituted C_2-C_{20} alkynyl group, and a substituted or unsubstituted C_3-C_{20} acyl group.

34. The method of claim **33** wherein R^9 is a hydrogen or a C_1-C_{10} substituted or unsubstituted alkyl group.

35. The method of claim **26** wherein said dopant provided to the analyzer is a substituted phenol having the formula:

(F3)



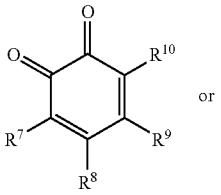
wherein R^{10} is selected from the group consisting of a hydrogen, a halogen, CN, OR, COOR, OCOOR, COR, $N(R)_2$, SR, SO_2R, SOR, a substituted or unsubstituted C_1-C_{20} alkyl group, a substituted or unsubstituted C_2-C_{20} alkenyl group, a substituted or unsubstituted C_2-C_{20} alkynyl group, a substituted or unsubstituted C_1-C_{20} alkoxy group, and a substituted or unsubstituted C_4-C_{20} aryl group; and wherein each R, independent of any other R in any listed group, is selected from H, a substituted or unsubstituted C_1-C_{20} alkyl group, a substituted or unsubstituted C_4-C_{20} aryl group, a substituted or unsubstituted C_2-C_{20} alkenyl group, a substituted or unsubstituted C_2-C_{20} alkynyl group, and a substituted or unsubstituted C_3-C_{20} acyl group.

36. The method of claim **35** wherein R^{10} is a hydrogen or a C_1-C_{10} substituted or unsubstituted alkyl group.

37. The method of claim **26** wherein said dopant provided to the analyzer is methyl salicylate or is 2-hydroxyacetophenone.

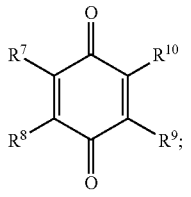
38. The method of claim **26** wherein said dopant provided to the analyzer is a substituted or unsubstituted quinone having the formula:

(F6)



or

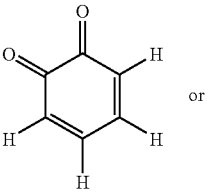
(F7)



wherein each of R^7, R^8, R^9 and R^{10} is independently selected from the group consisting of: a hydrogen, a halogen, CN, OR, COOR, OCOOR, COR, $N(R)_2$, SR, SO_2R, SOR, a substituted or unsubstituted C_1-C_{20} alkyl group, a substituted or unsubstituted C_2-C_{20} alkenyl group, a substituted or unsubstituted C_2-C_{20} alkynyl group, a substituted or unsubstituted C_1-C_{20} alkoxy group, and a substituted or unsubstituted C_4-C_{20} aryl group; wherein each R, independent of any other R in any listed group, is selected from H, a substituted or unsubstituted C_1-C_{20} alkyl group, a substituted or unsubstituted C_4-C_{20} aryl group, a substituted or unsubstituted C_2-C_{20} alkenyl group, a substituted or unsubstituted C_2-C_{20} alkynyl group, and a substituted or unsubstituted C_3-C_{20} acyl group.

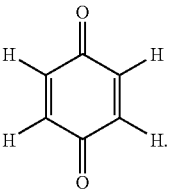
39. The method of claim **26** wherein said dopant provided to the analyzer is a quinone having the formula:

(F8)



or

(F9)



40. The method of claim **26** wherein said step of providing dopant to said ionization region provides detection conditions wherein analyte ions have drift times that are distinguishable from the drift times of ions generated from water in said analyzer.

41. The method of claim **26** wherein the concentration of dopant provided to said ionization region, separation region or both is selected from the range of 1 ppm to 100 ppm.

42. The method of claim **26** wherein said step of detecting said analyte ions separated on the basis of ion mobility comprises detecting one or more peroxide analytes selected from the group consisting of hydrogen peroxide, a hydroperoxide, and an organic peroxide.

43. A method of suppressing interference from water vapor in an ion mobility spectrometry analyzer, said method comprising:

providing an ion mobility spectrometry analyzer having an inlet, ionization region, separation region and detector;

passing at least a portion of a sample having peroxide analytes through said inlet of said analyzer into said ionization region of said analyzer; and

providing dopant to said ionization region, separation region or both of said analyzer, wherein said dopant is a substituted aryl compound or a substituted cyclic diene; wherein the substituted aryl compound or substituted cyclic diene has at least one substituent selected from the group consisting of a hydroxyl group, a carbonyl group, an aldehyde group, an ester group, a carboxylic acid group and a carbonate ester group;

wherein said dopant provided to said ionization region, separation region or both of said analyzer suppresses interference from water vapor in said ion mobility spectrometry analyzer.

* * * * *