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(54) RETRO-REGRESSION RESIDUAL REMEDIATION FOR SPECTRAL/SIGNAL IDENTIFICATION

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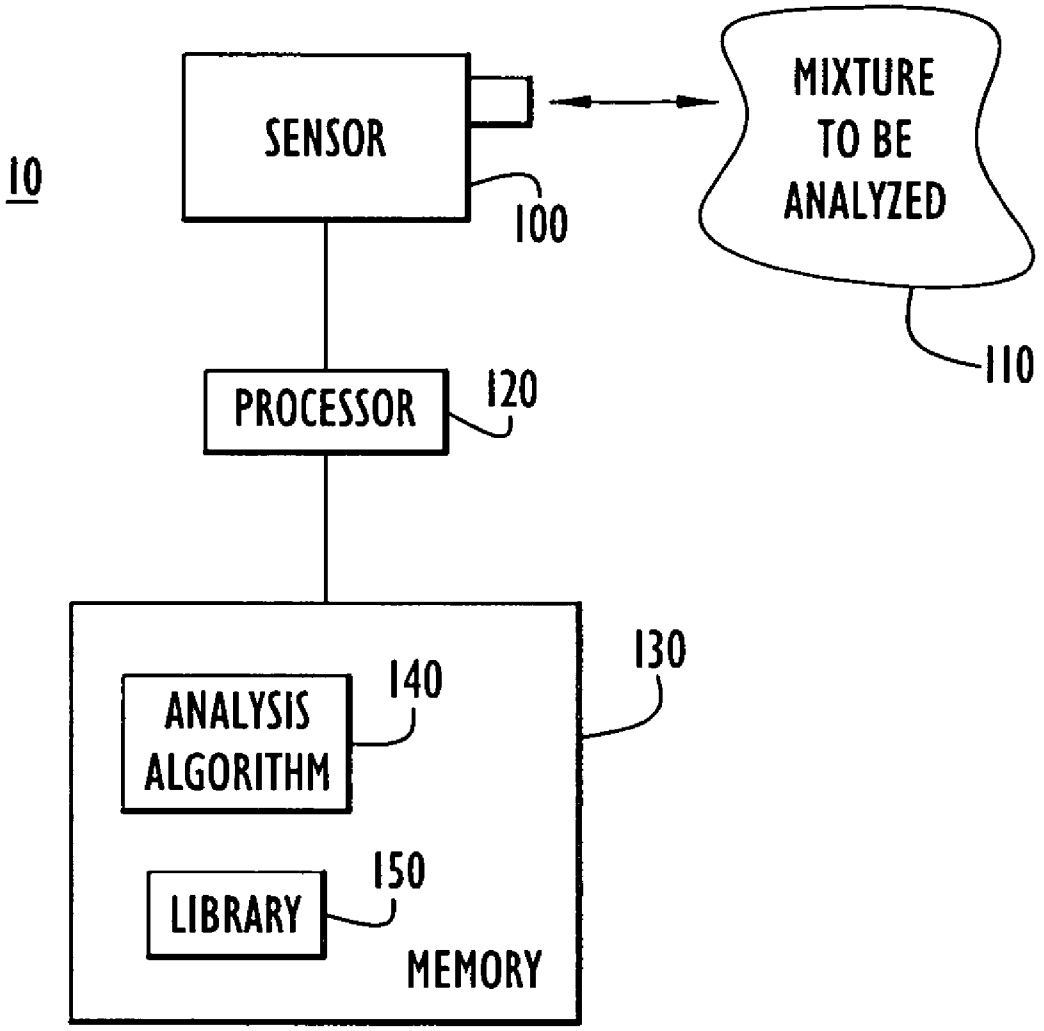
(57) ABSTRACT

An improved regression-based qualitative analysis algorithm useful when the mixture to be analyzed contains a compound not in the library spectra, a so-called unknown. A regression of a measured spectrum is computed against the library spectra. This regression is referred to as a "master" regression. Estimated mixing coefficients for an estimated spectrum are computed from the regression. Next, a residual error is computed between the estimated spectrum and the measured spectrum. Peaks in the residual error are identified that extend in a direction opposite to that of peaks in the measured spectrum. These peaks are referred to as "negative" peaks. A regression is performed on the peaks. This is referred to as a "retro-regression" to be distinguished from the master regression performed on the measured spectrum. Using information from the retro-regression, corrected mixing coefficients are computed and the process repeats.



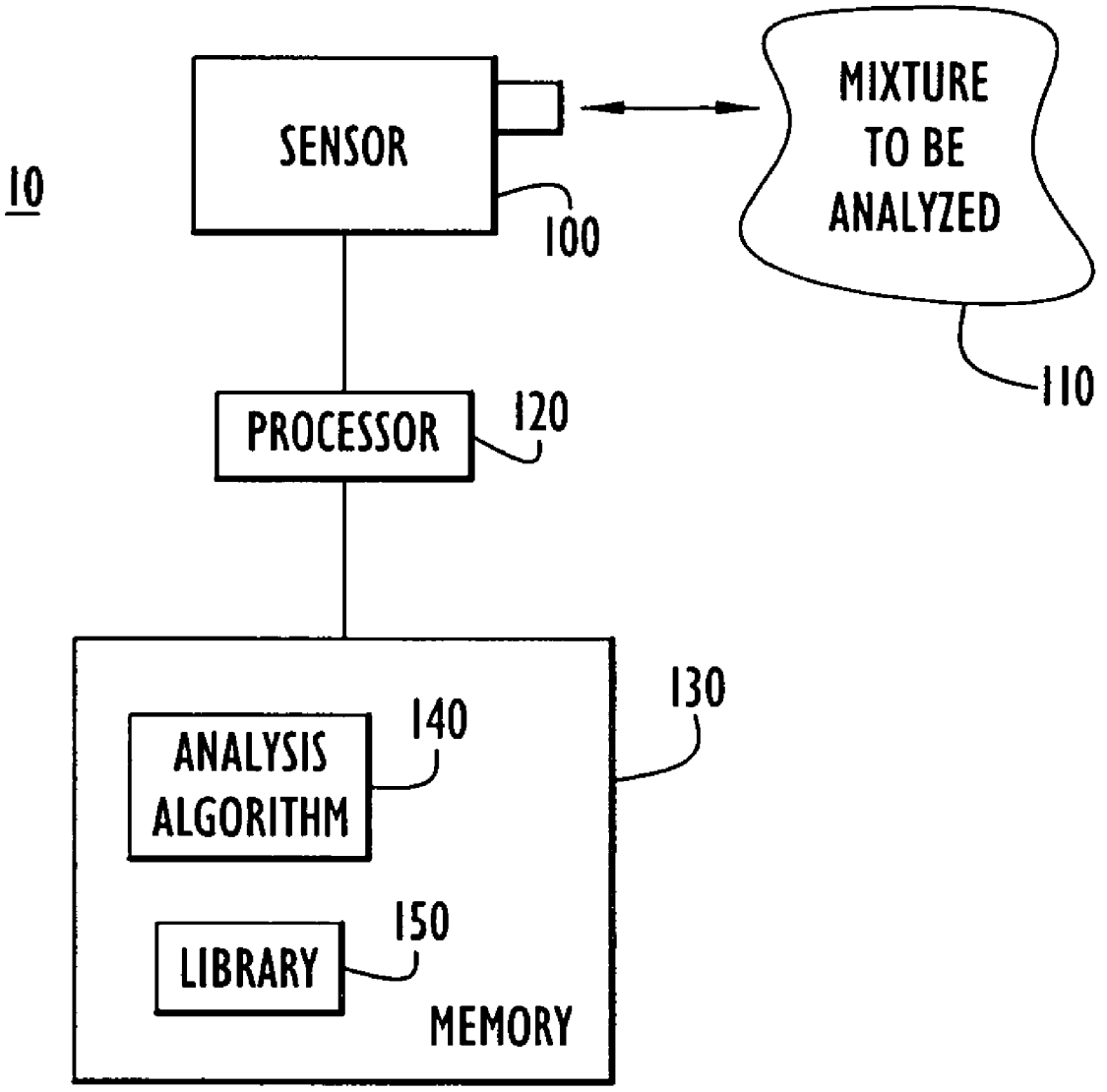

10
SENSOR
100
MIXTURE TO BE ANALYZED
110
PROCESSOR
120
130
ANALYSIS ALGORITHM
140
LIBRARY
150
MEMORY

FIG.1

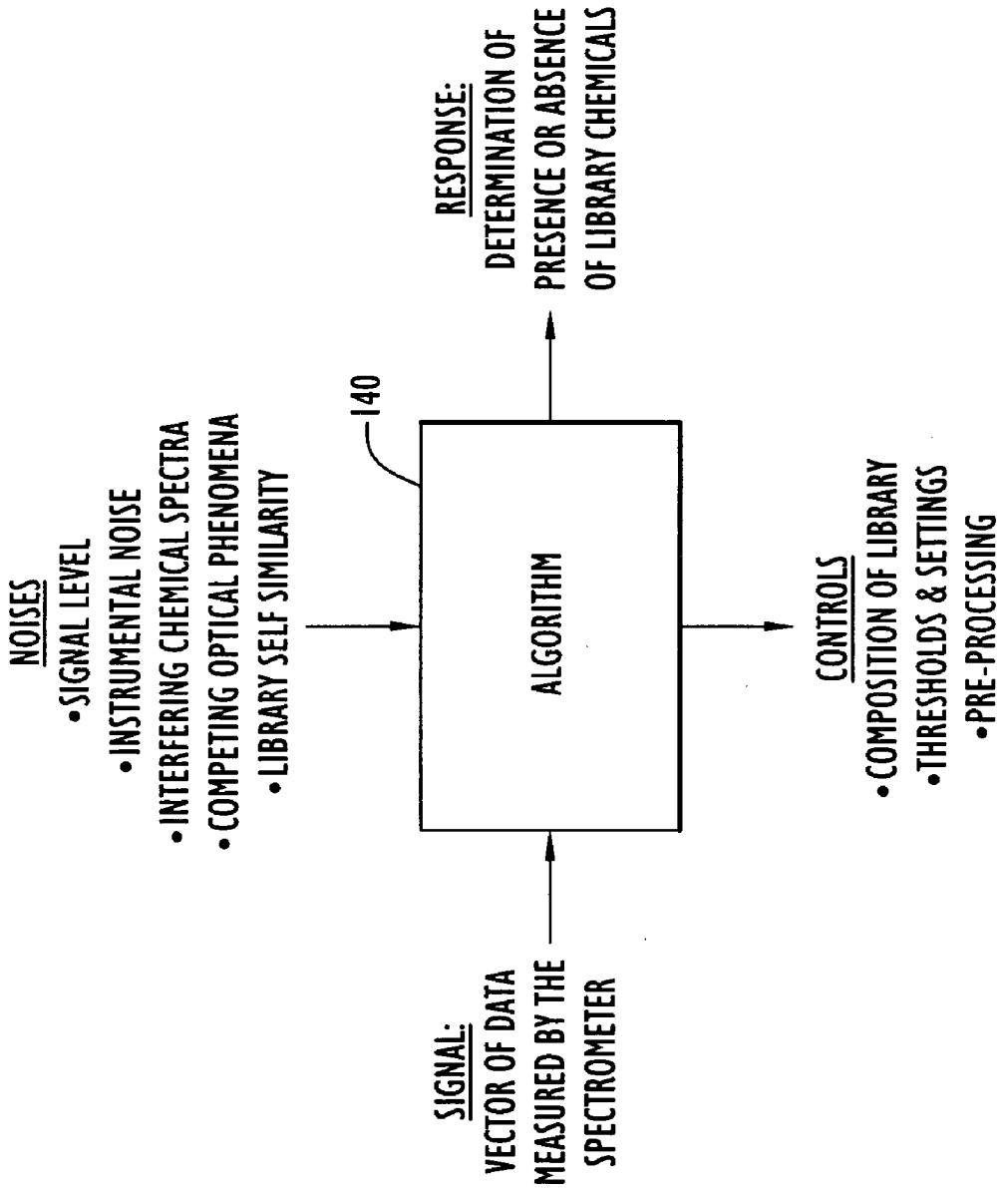
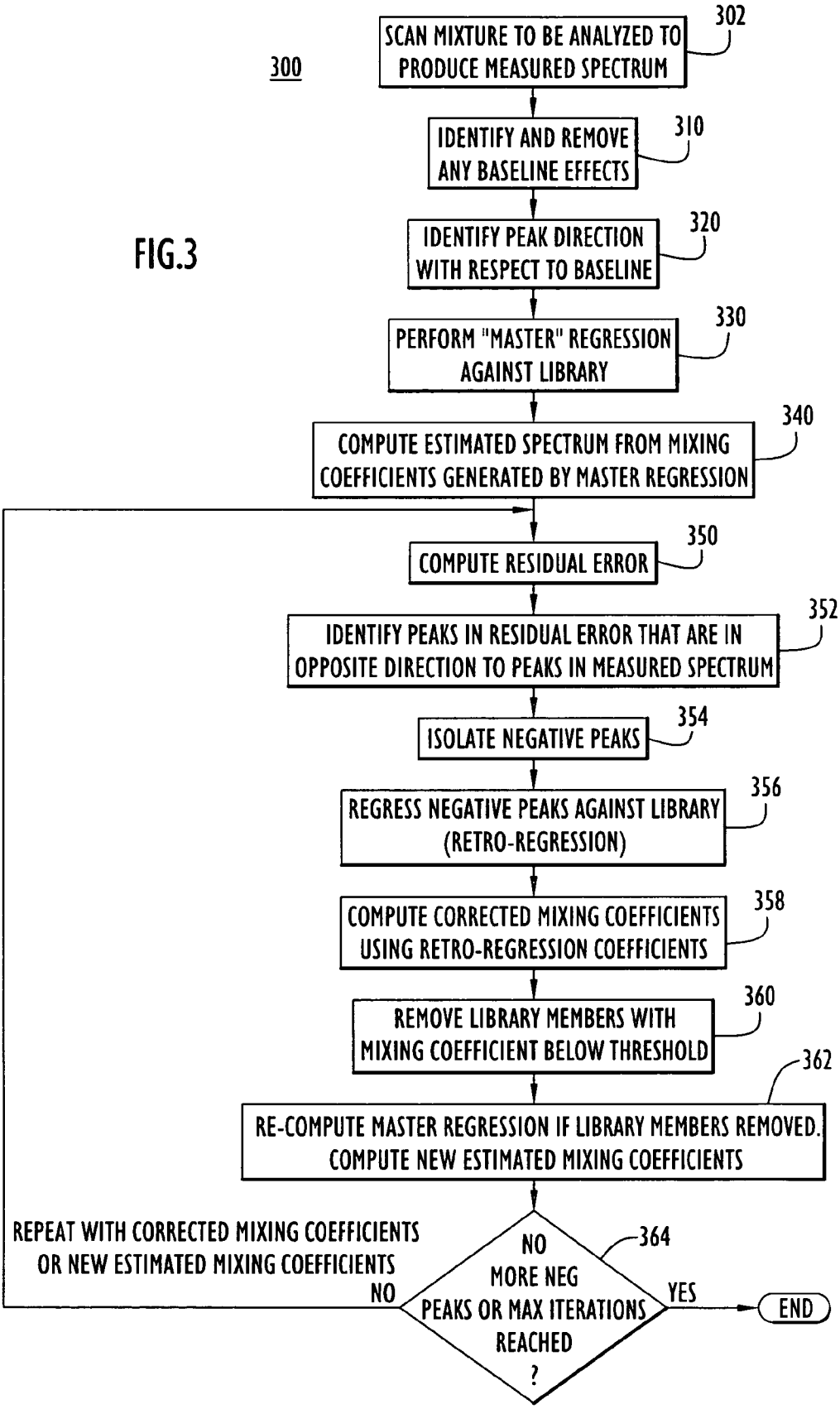

NOISES
•SIGNAL LEVEL
•INSTRUMENTAL NOISE
•INTERFERING CHEMICAL SPECTRA
•COMPETING OPTICAL PHENOMENA
•LIBRARY SELF SIMILARITY
140
ALGORITHM
RESPONSE:
DETERMINATION OF
PRESENCE OR ABSENCE
OF LIBRARY CHEMICALS
CONTROLS
•COMPOSITION OF LIBRARY
•THRESHOLDS & SETTINGS
•PRE-PROCESSING
SIGNAL:
VECTOR OF DATA
MEASURED BY THE
SPECTROMETER

FIG.2

FIG.3


300
SCAN MIXTURE TO BE ANALYZED TO PRODUCE MEASURED SPECTRUM
302
IDENTIFY AND REMOVE ANY BASELINE EFFECTS
310
IDENTIFY PEAK DIRECTION WITH RESPECT TO BASELINE
320
PERFORM "MASTER" REGRESSION AGAINST LIBRARY
330
COMPUTE ESTIMATED SPECTRUM FROM MIXING COEFFICIENTS GENERATED BY MASTER REGRESSION
340
COMPUTE RESIDUAL ERROR
350
IDENTIFY PEAKS IN RESIDUAL ERROR THAT ARE IN OPPOSITE DIRECTION TO PEAKS IN MEASURED SPECTRUM
352
ISOLATE NEGATIVE PEAKS
354
REGRESS NEGATIVE PEAKS AGAINST LIBRARY (RETRO-REGRESSION)
356
COMPUTE CORRECTED MIXING COEFFICIENTS USING RETRO-REGRESSION COEFFICIENTS
358
REMOVE LIBRARY MEMBERS WITH MIXING COEFFICIENT BELOW THRESHOLD
360
RE-COMPUTE MASTER REGRESSION IF LIBRARY MEMBERS REMOVED. COMPUTE NEW ESTIMATED MIXING COEFFICIENTS
362
NO MORE NEG PEAKS OR MAX ITERATIONS REACHED ?
364
YES
END
NO
REPEAT WITH CORRECTED MIXING COEFFICIENTS OR NEW ESTIMATED MIXING COEFFICIENTS

2clbutane	2clpropane	cn
cr	cs	cx
dem	ep	ga
gb	gd	gf
hd	hn	hq
ht	m xylene	mdea
mes	mp	xylene
p xylene	acetone	acetonitrile
acrolein	acrylonitrile	benzene
chloroethylether	chloropicrin	cyclohexane
dibenzosuberone	dichloroethene	ethanol
ethylene	formalehyde	hexane
hydrazine l	spropanol	methanol
nicotine	pentane	tetrafluoroethene
thf	toluene	

Chemicals in the Library

FIG. 4

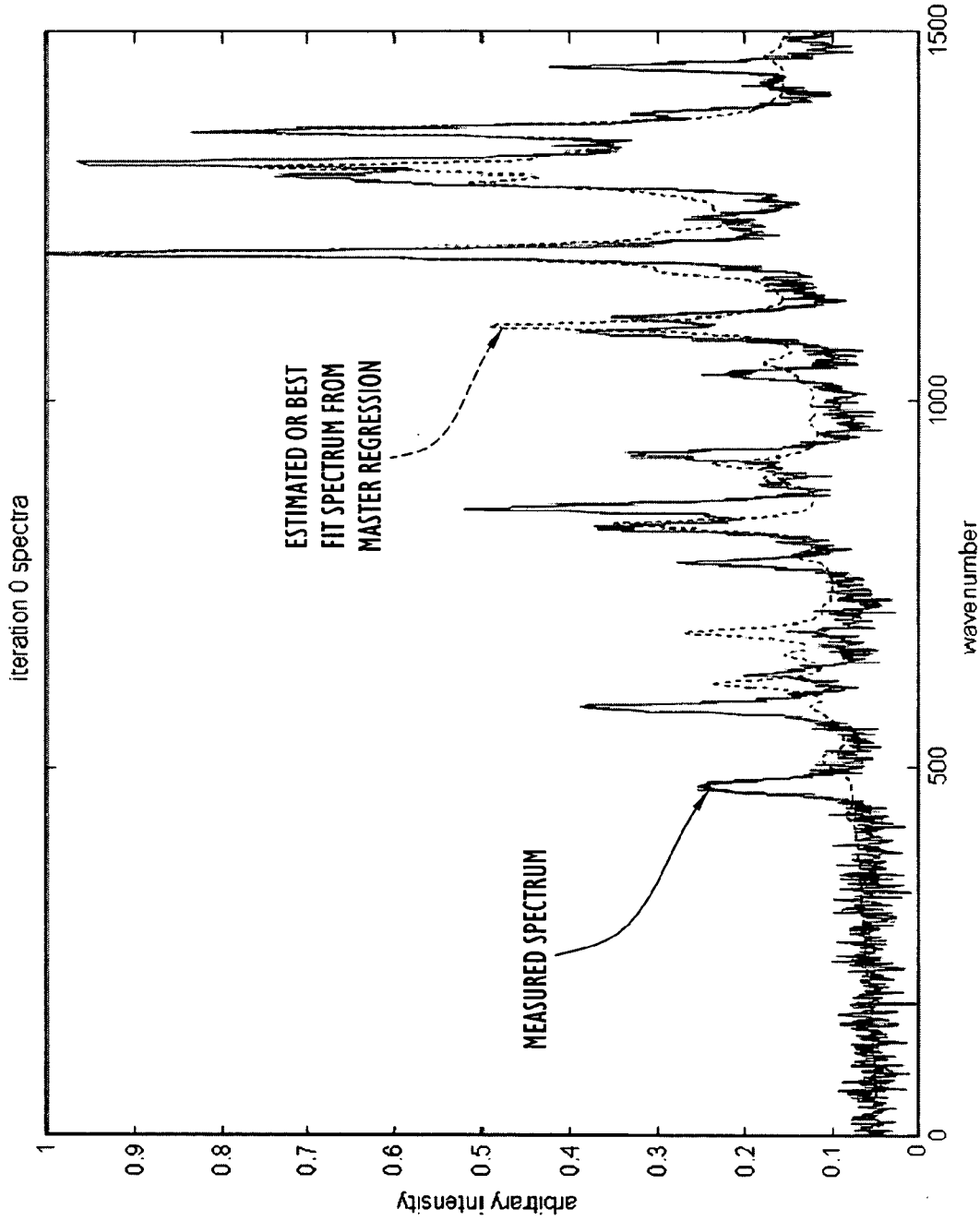

iteration 0 spectra
ESTIMATED OR BEST
FIT SPECTRUM FROM
MASTER REGRESSION
MEASURED SPECTRUM
arbitrary intensity
wavenumber
0
0.1
0.2
0.3
0.4
0.5
0.6
0.7
0.8
0.9
1
0
500
1000
1500

FIG.5A

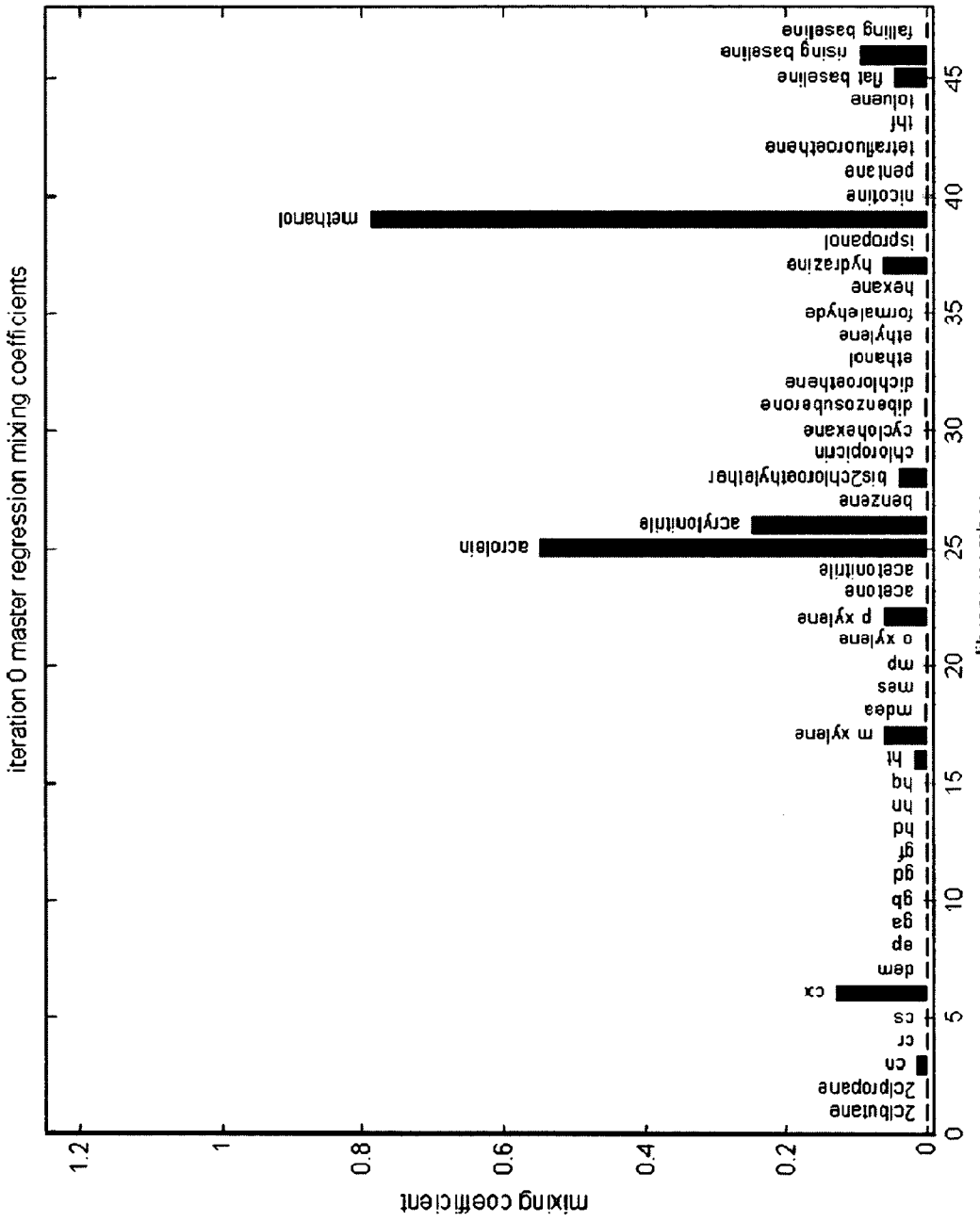

iteration 0 master regression mixing coefficients
mixing coefficient
library member
2clbutane
2clpropane
cn
cr
cs
cx
dem
ep
ga
gb
gd
gf
hd
hn
hq
ht
m xylene
mdea
mes
mp
o xylene
p xylene
acetone
acetonitrile
acrolein
acrylonitrile
benzene
bis2chloroethylether
chloropicrin
cyclohexane
dibenzosuberone
dichloroethene
ethanol
ethylene
formaldehyde
hexane
hydrazine
isopropanol
methanol
nicotine
pentane
tetrafluoroethene
thf
toluene
flat baseline
rising baseline
falling baseline

FIG.5B

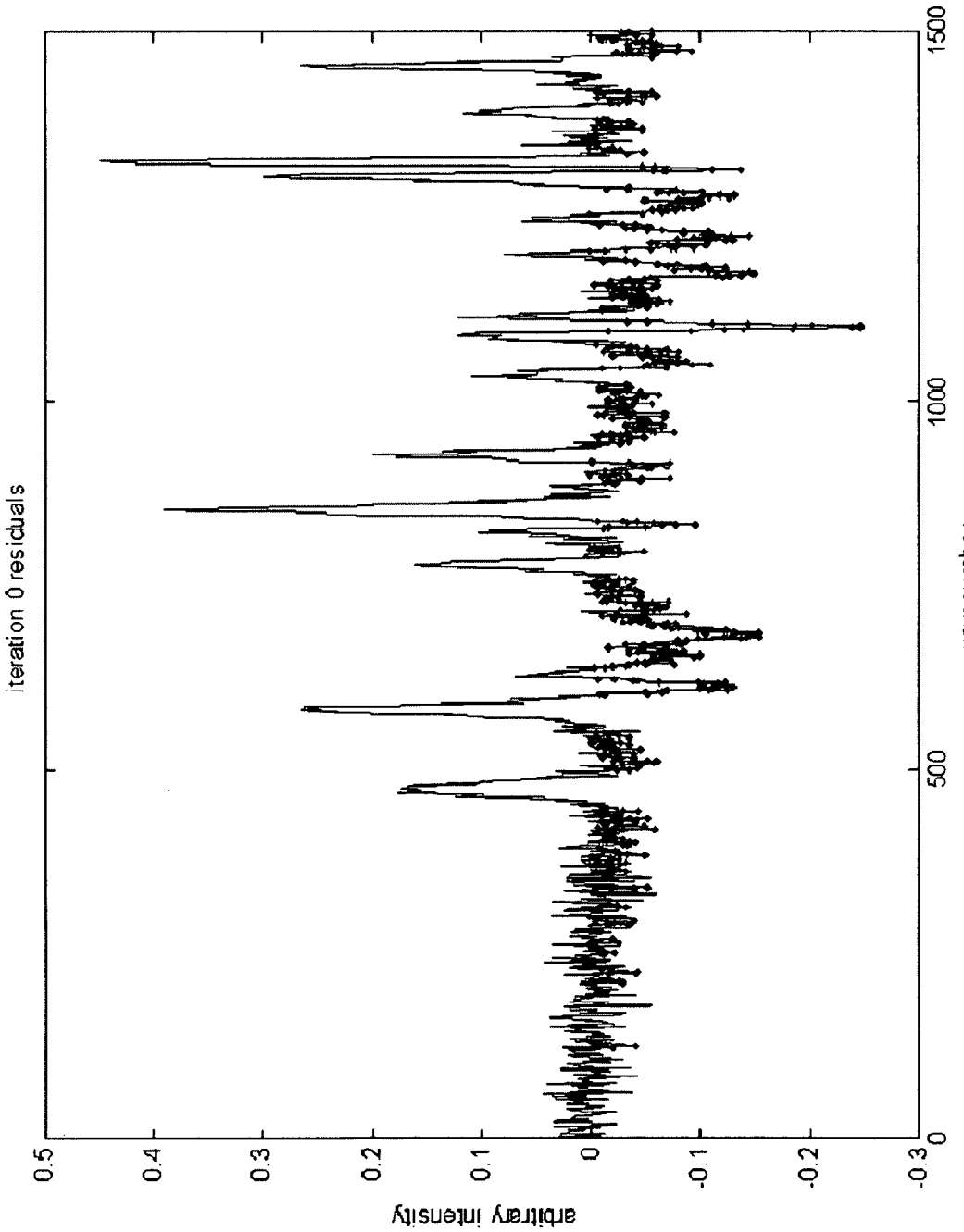

iteration 0 residuals
arbitrary intensity
0.5
0.4
0.3
0.2
0.1
0
-0.1
-0.2
-0.3
0
500
1000
1500
wavenumber

FIG.5C

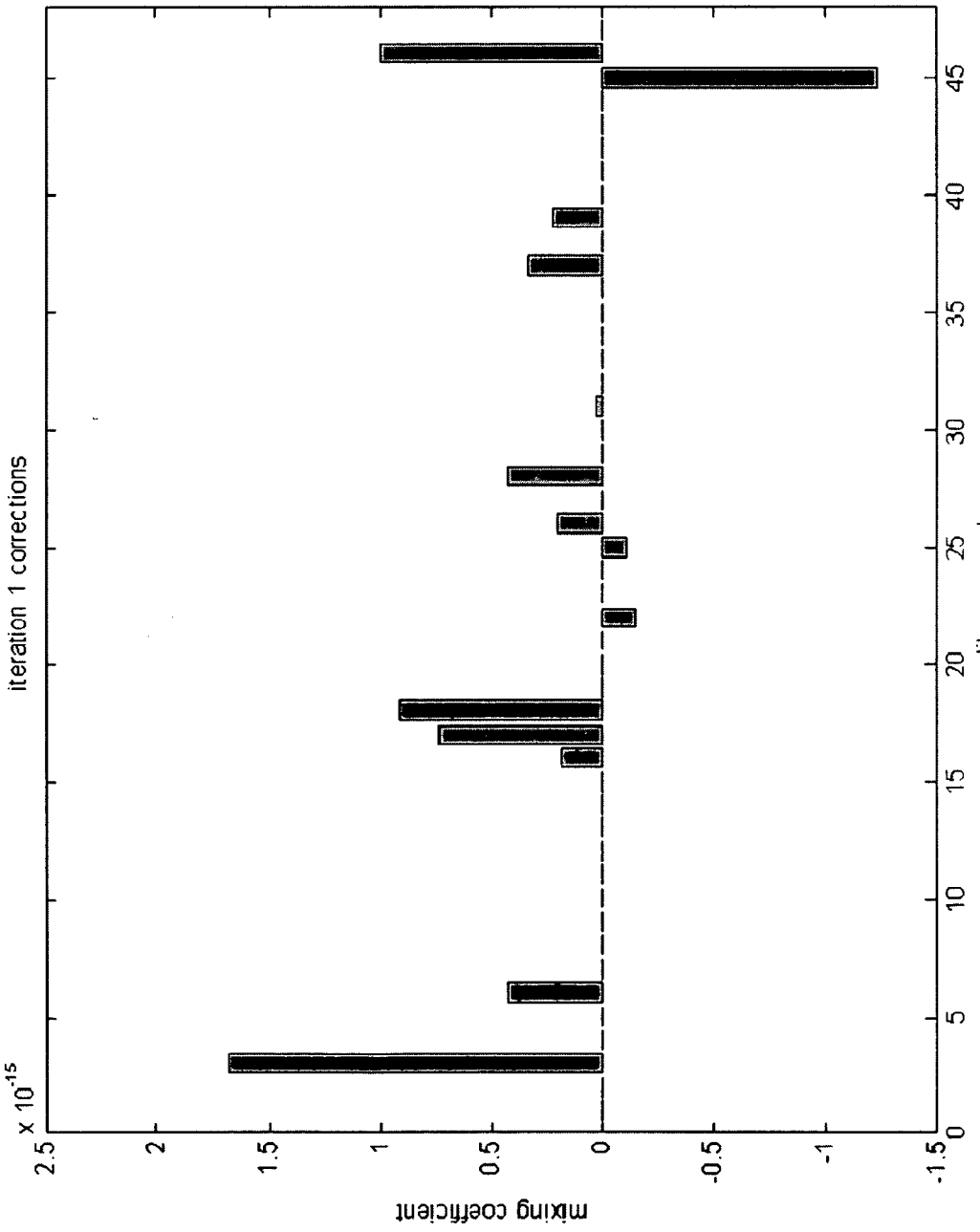

iteration 1 corrections
x 10^-15
2.5
2
1.5
1
0.5
0
-0.5
-1
-1.5
mixing coefficient
0
5
10
15
20
25
30
35
40
45
library member

FIG.6A

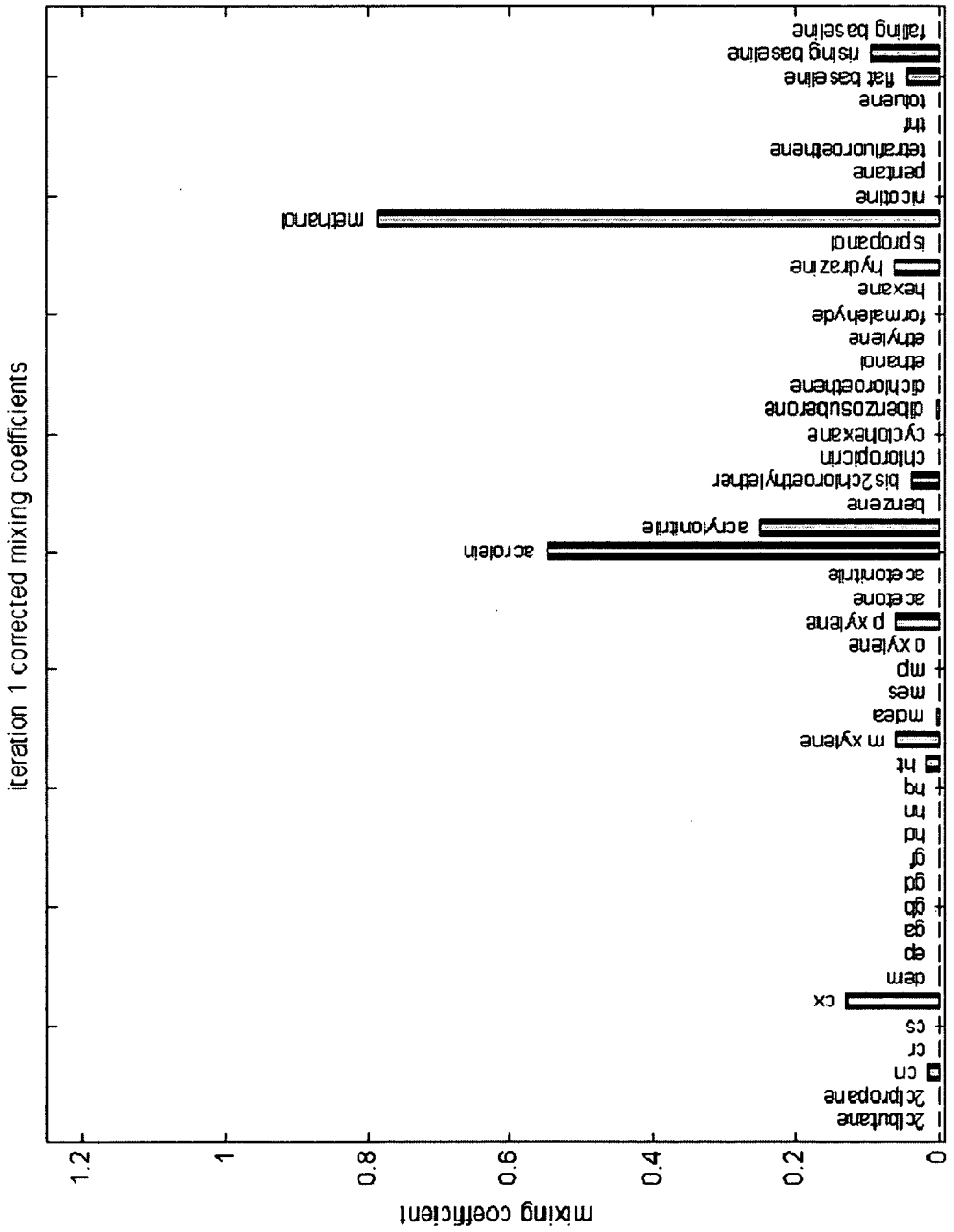

iteration 1 corrected mixing coefficients
mixing coefficient
library member
0
0.2
0.4
0.6
0.8
1
1.2
5
10
15
20
25
30
35
40
45
2c1butane
2c1propane
cn
cr
cs
cx
dem
ep
ga
gb
gd
gf
hd
hn
hq
ht
m xylene
mdea
mes
mp
o xylene
p xylene
acetone
acetonitrile
acrolein
acrylonitrile
benzene
bis2chloroethylether
chloropicrin
cyclohexane
dibenzosuberone
dichloroethene
ethanol
ethylene
formaldehyde
hexane
hydrazine
isopropanol
methanol
nicotine
pentane
tetrafluoroethene
thf
toluene
flat baseline
rising baseline
falling baseline

FIG.6B

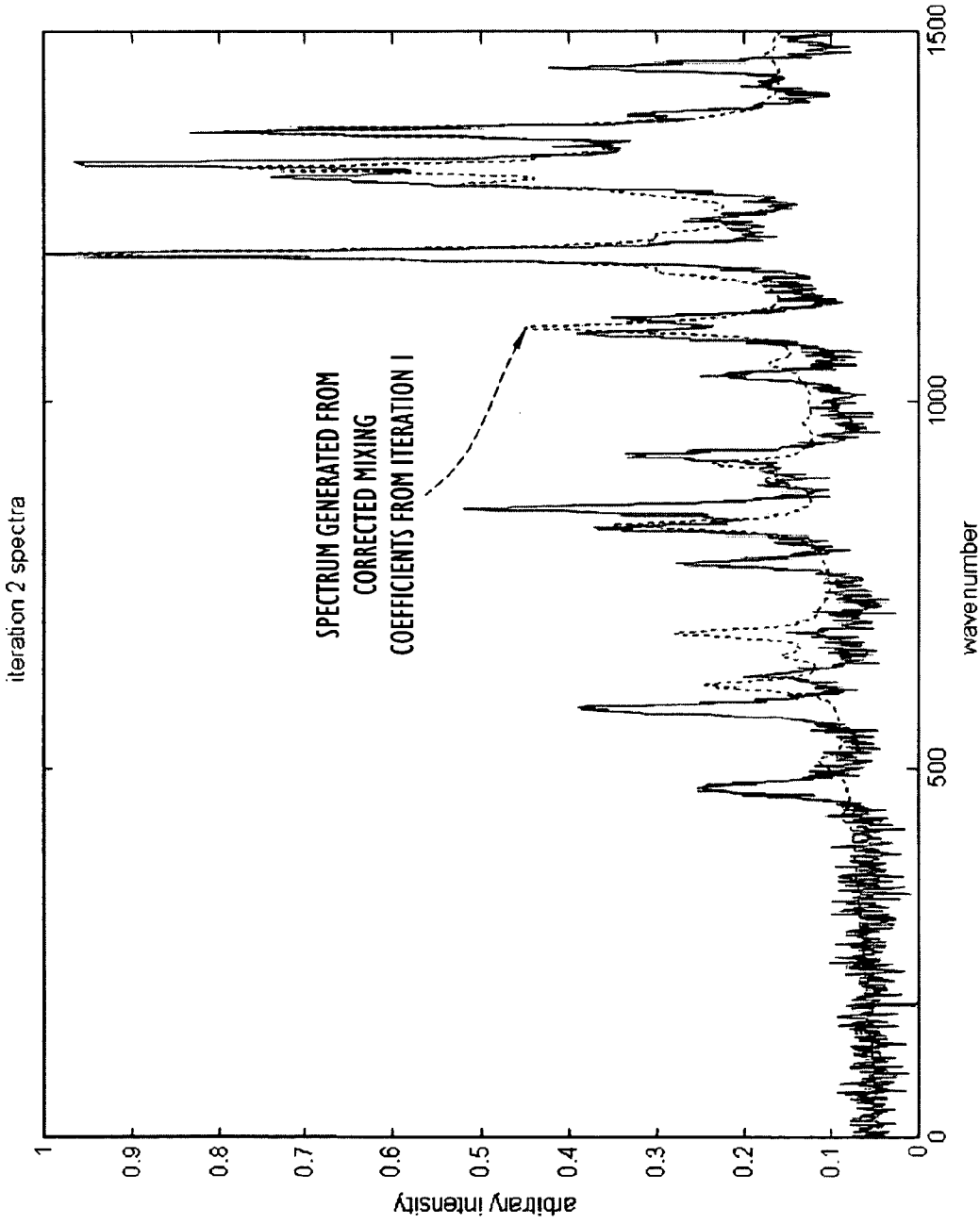

iteration 2 spectra
SPECTRUM GENERATED FROM
CORRECTED MIXING
COEFFICIENTS FROM ITERATION 1
arbitrary intensity
wave number
0
0.1
0.2
0.3
0.4
0.5
0.6
0.7
0.8
0.9
1
500
1000
1500

FIG.7A

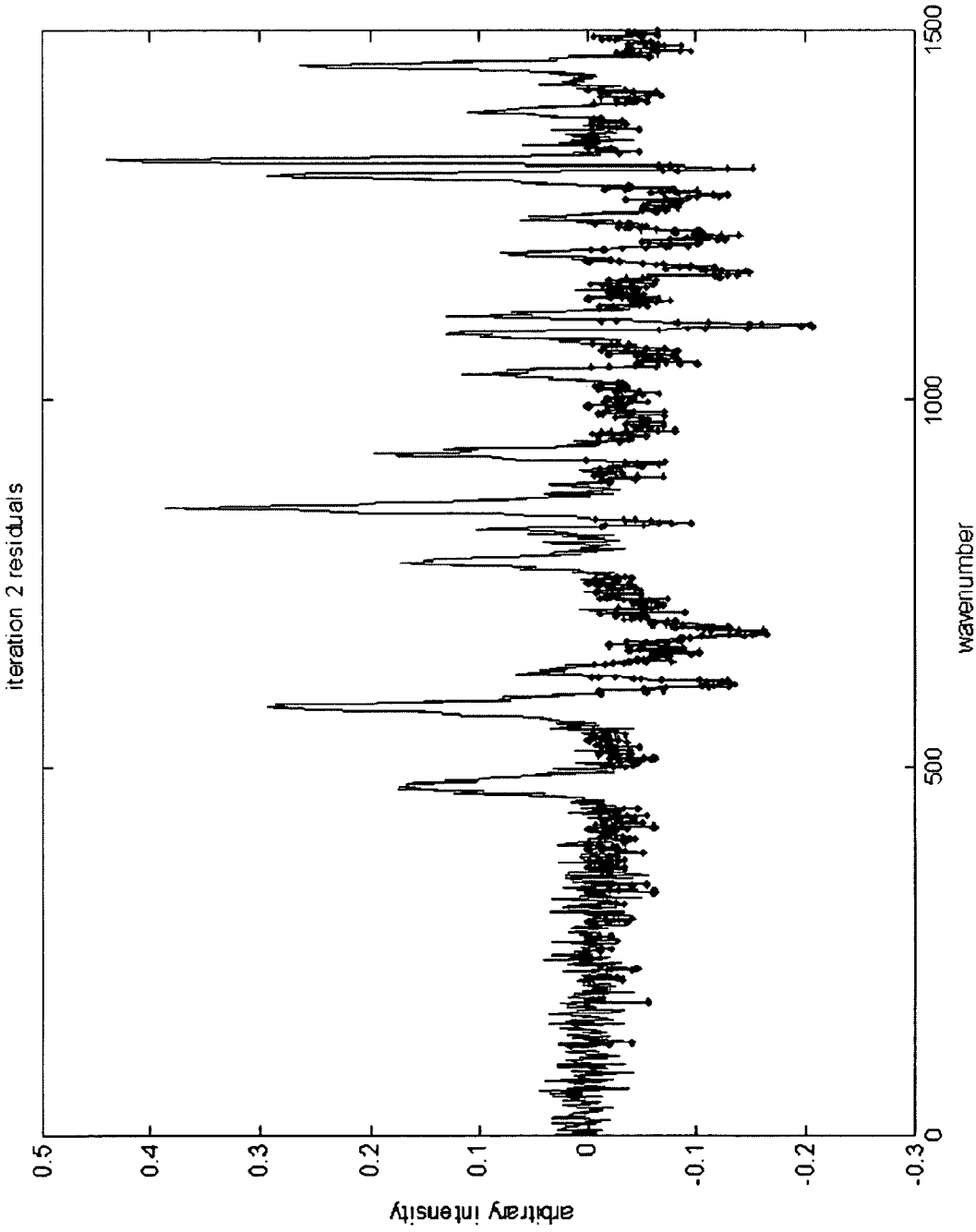

iteration 2 residuals
arbitrary intensity
wavenumber
0.5
0.4
0.3
0.2
0.1
0
-0.1
-0.2
-0.3
0
500
1000
1500

FIG.7B

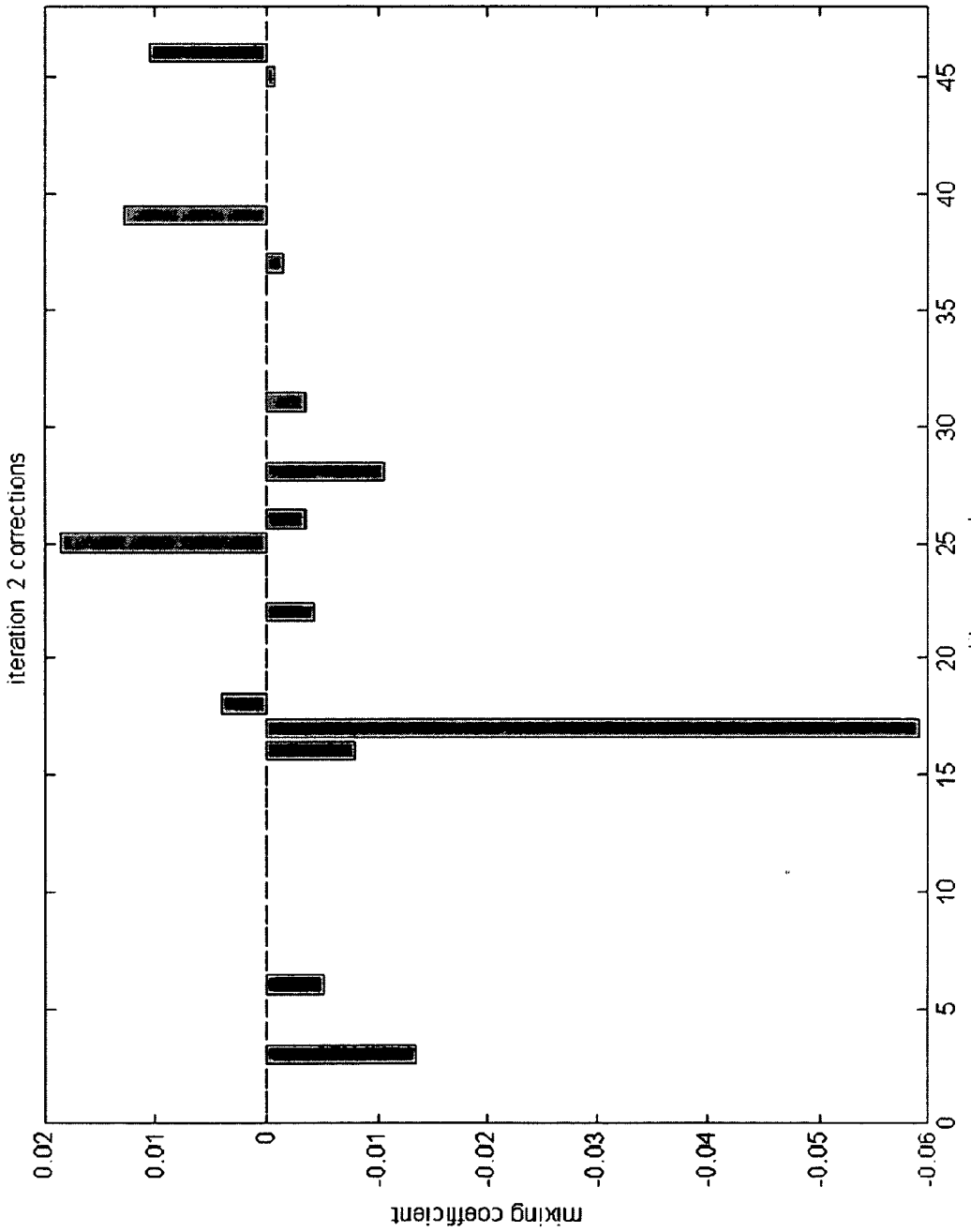

iteration 2 corrections
mixing coefficient
library member
0.02
0.01
0
-0.01
-0.02
-0.03
-0.04
-0.05
-0.06
0
5
10
15
20
25
30
35
40
45

FIG.7C

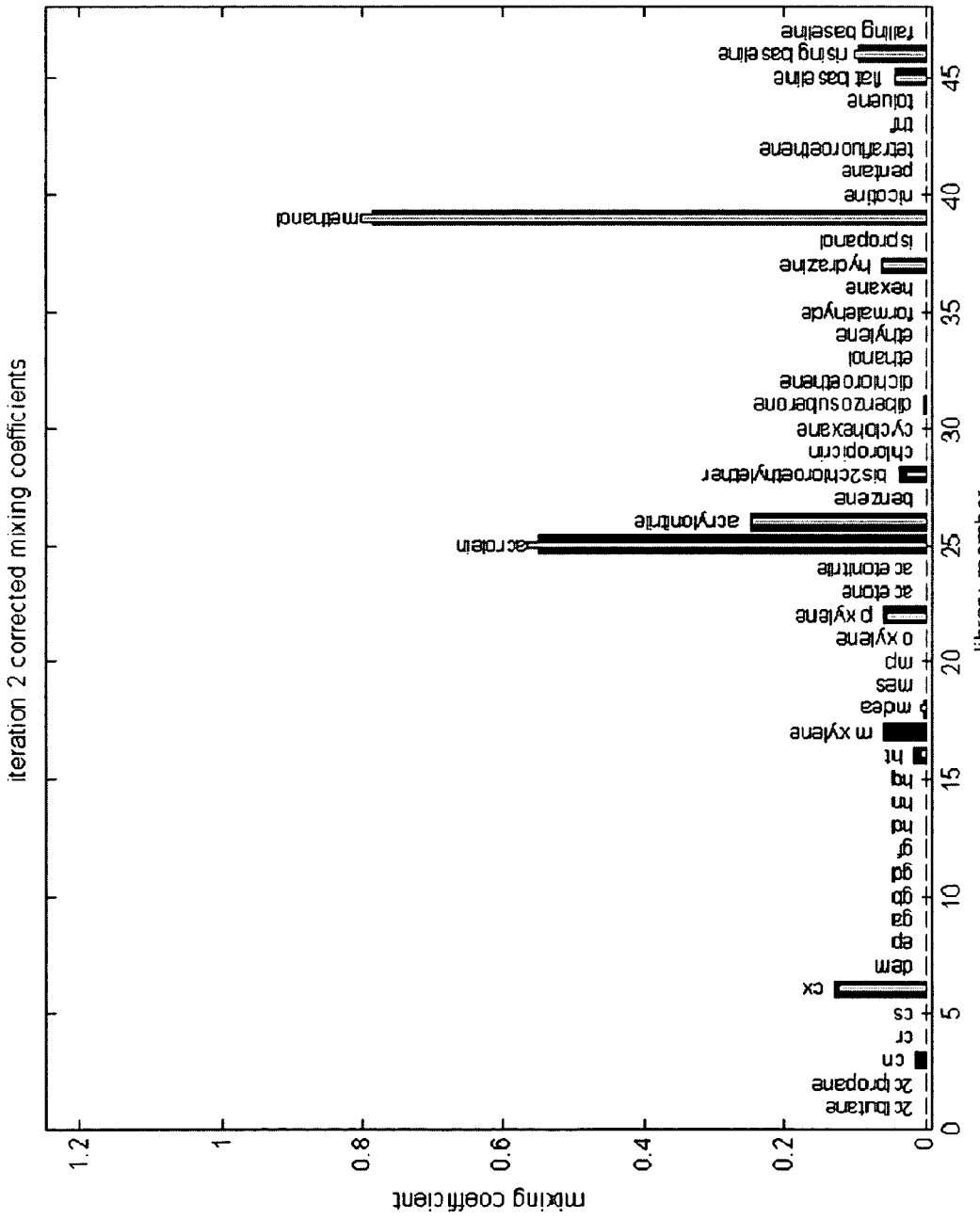

iteration 2 corrected mixing coefficients
mixing coefficient
library member
2c butane
2c propane
cn
cr
cs
cx
dem
ep
ga
gb
gd
ha
hn
hq
ht
m xylene
mdea
mes
mp
o xylene
p xylene
ac etone
ac etonitrile
acrolein
acrylonitrile
benzene
bis2chloroethylether
chloropicrin
cyclohexane
dibenzosuberone
dichloroethene
ethanol
ethylene
formalehyde
hexane
hydrazine
isopropanol
methanol
nicotine
pentane
tetrafluoroethene
trr
toluene
flat baseline
rising baseline
falling baseline

FIG.7D

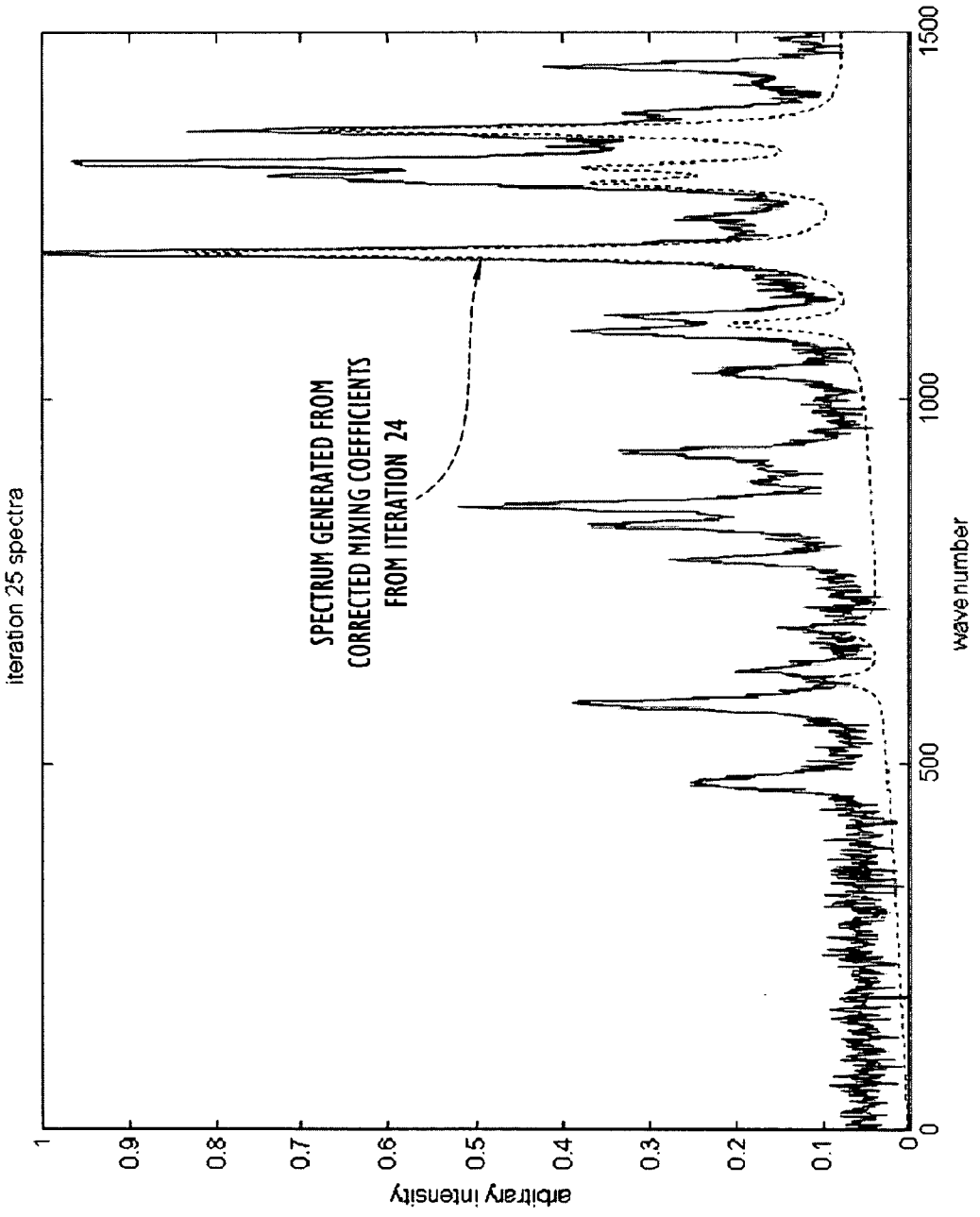

iteration 25 spectra
SPECTRUM GENERATED FROM
CORRECTED MIXING COEFFICIENTS
FROM ITERATION 24
arbitrary intensity
wave number
0
0.1
0.2
0.3
0.4
0.5
0.6
0.7
0.8
0.9
1
0
500
1000
1500

FIG.8A

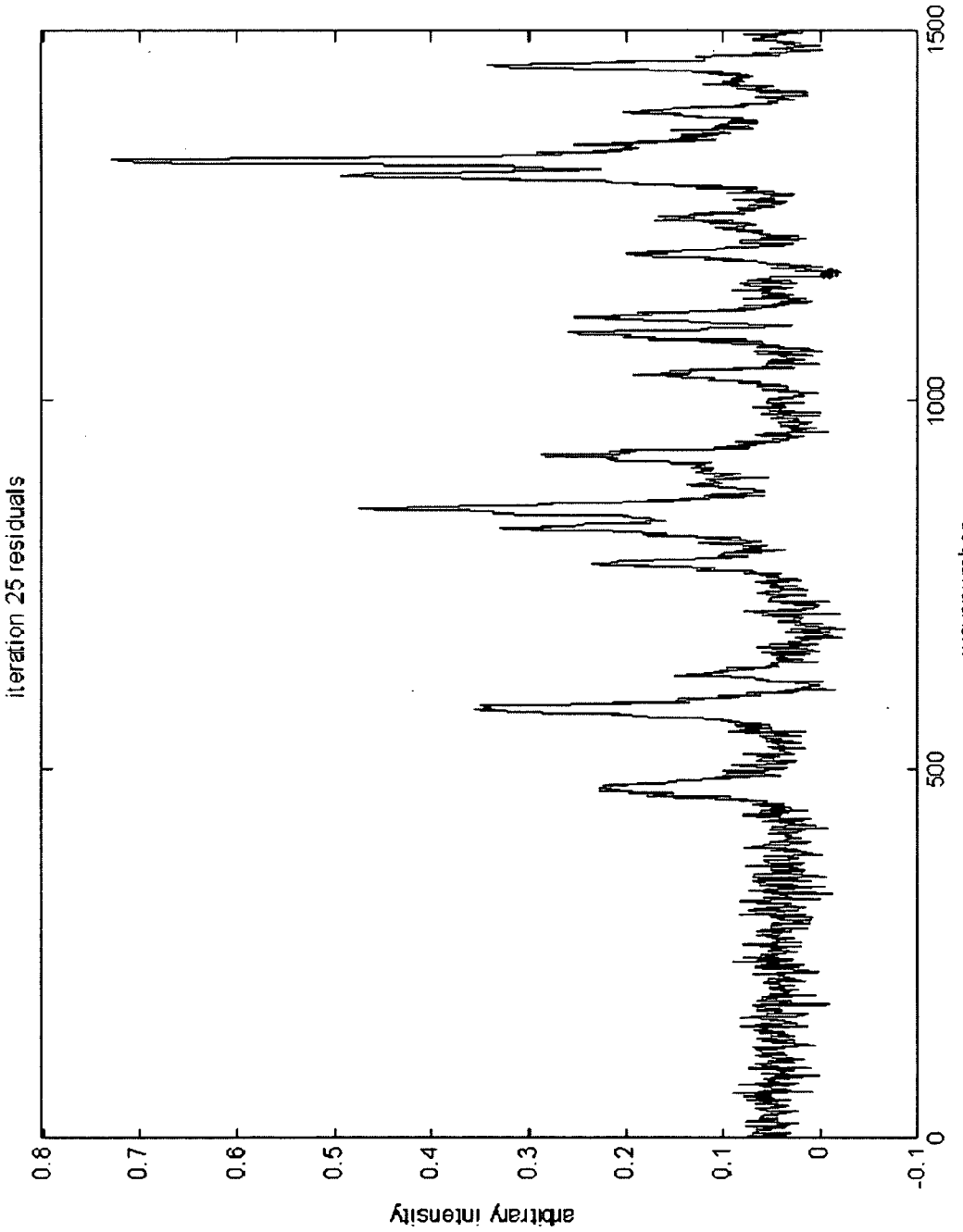

iteration 25 residuals
arbitrary intensity
wavenumber
0.8
0.7
0.6
0.5
0.4
0.3
0.2
0.1
0
-0.1
0
500
1000
1500

FIG.8B

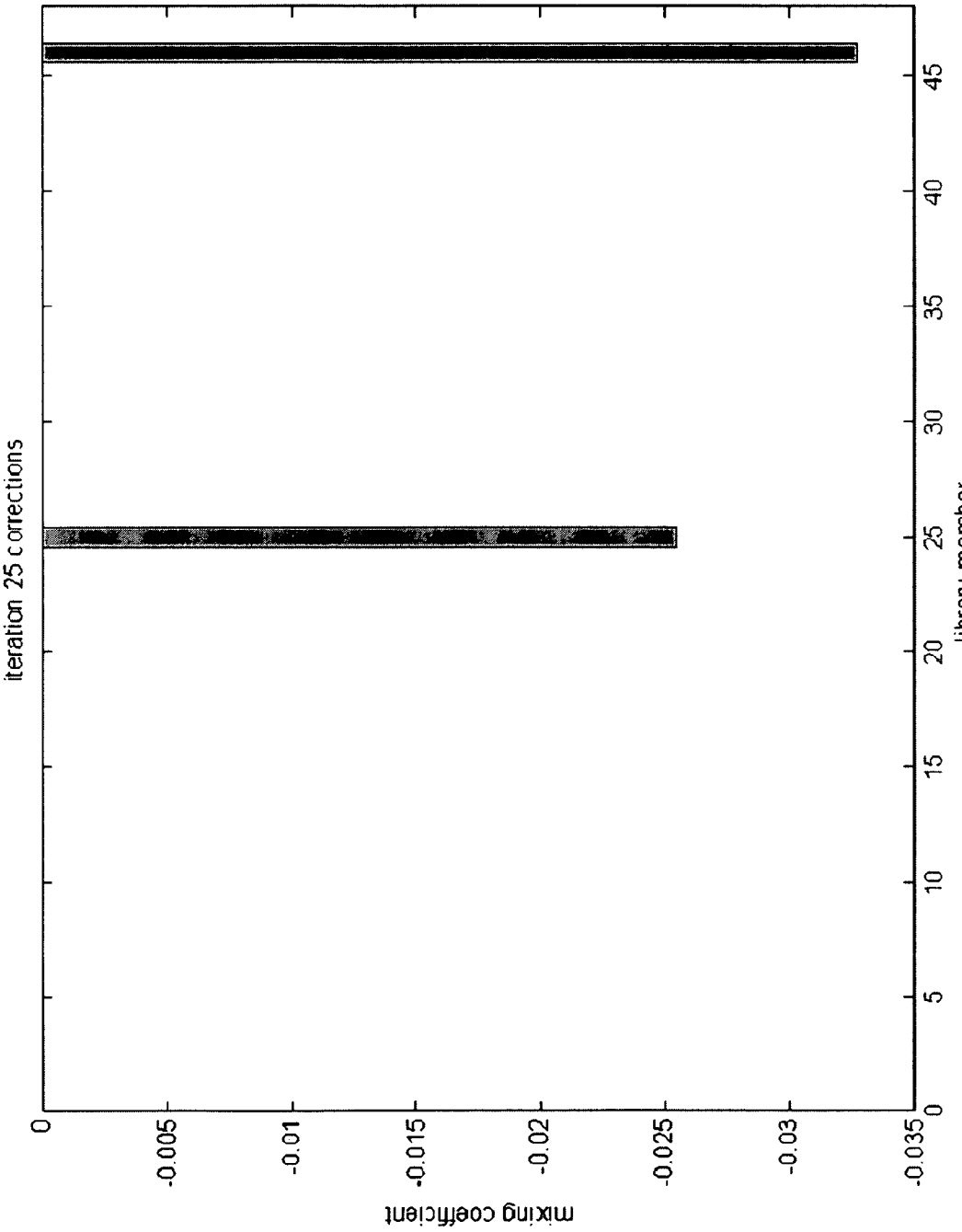

iteration 25 corrections
mixing coefficient
0
-0.005
-0.01
-0.015
-0.02
-0.025
-0.03
-0.035
0
5
10
15
20
25
30
35
40
45
library member

FIG.8C

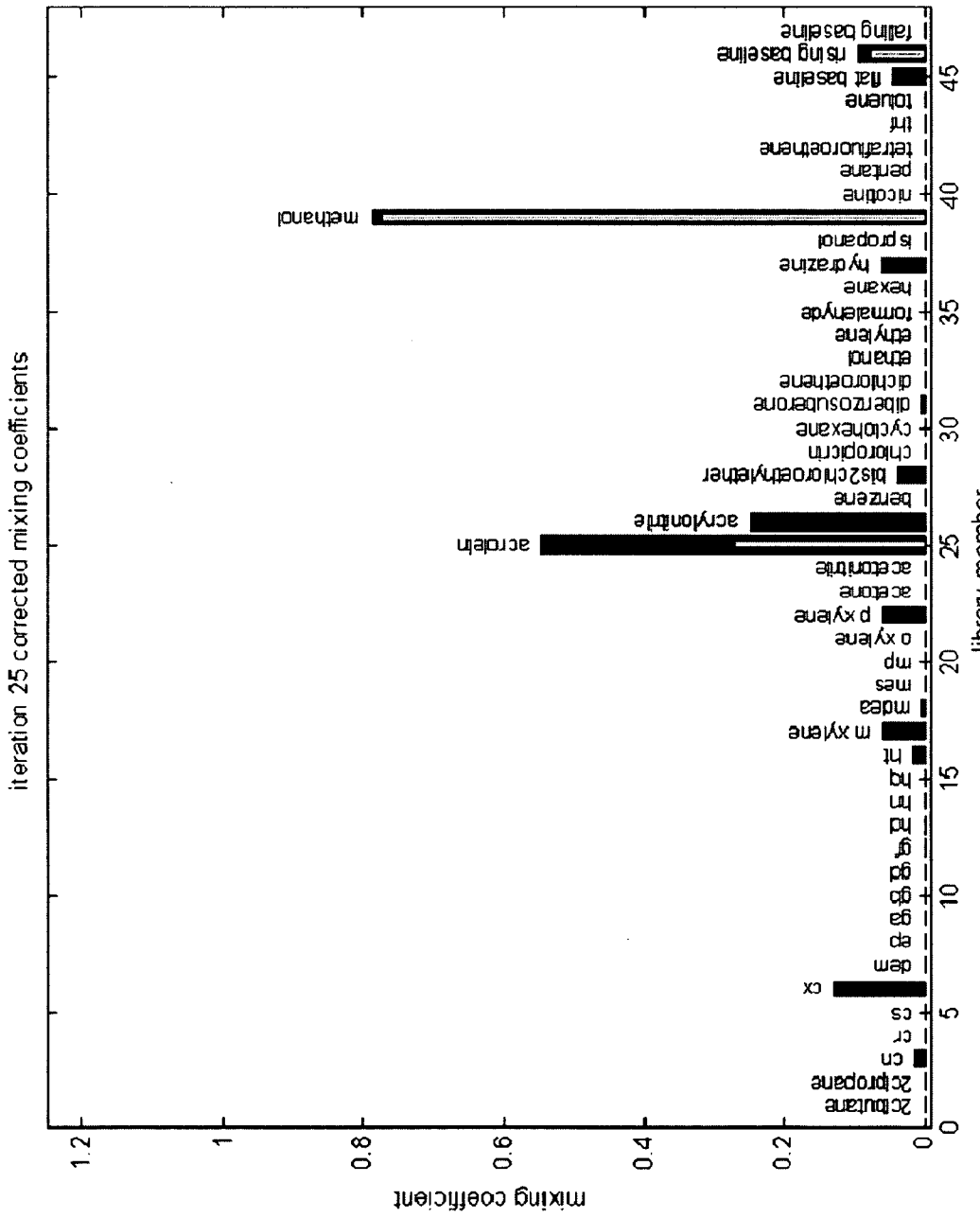

iteration 25 corrected mixing coefficients
mixing coefficient
library member
0
0.2
0.4
0.6
0.8
1
1.2
0
5
10
15
20
25
30
35
40
45
2ctbutane
2ctpropane
cn
cr
cs
cx
dem
ep
ga
gb
gd
gr
hd
hn
hq
ht
m xylene
mdea
mes
mp
o xylene
p xylene
acetone
acetonitrile
acrolein
acrylonitrile
benzene
bis2chloroethylether
chloropicrin
cyclohexane
diberzosuberone
dichloroethene
ethanol
ethylene
formalenyde
hexane
hydrazine
isopropanol
methanol
nicotine
pentane
tetrafluoroethene
thf
toluene
flat baseline
rising baseline
falling baseline

FIG.8D

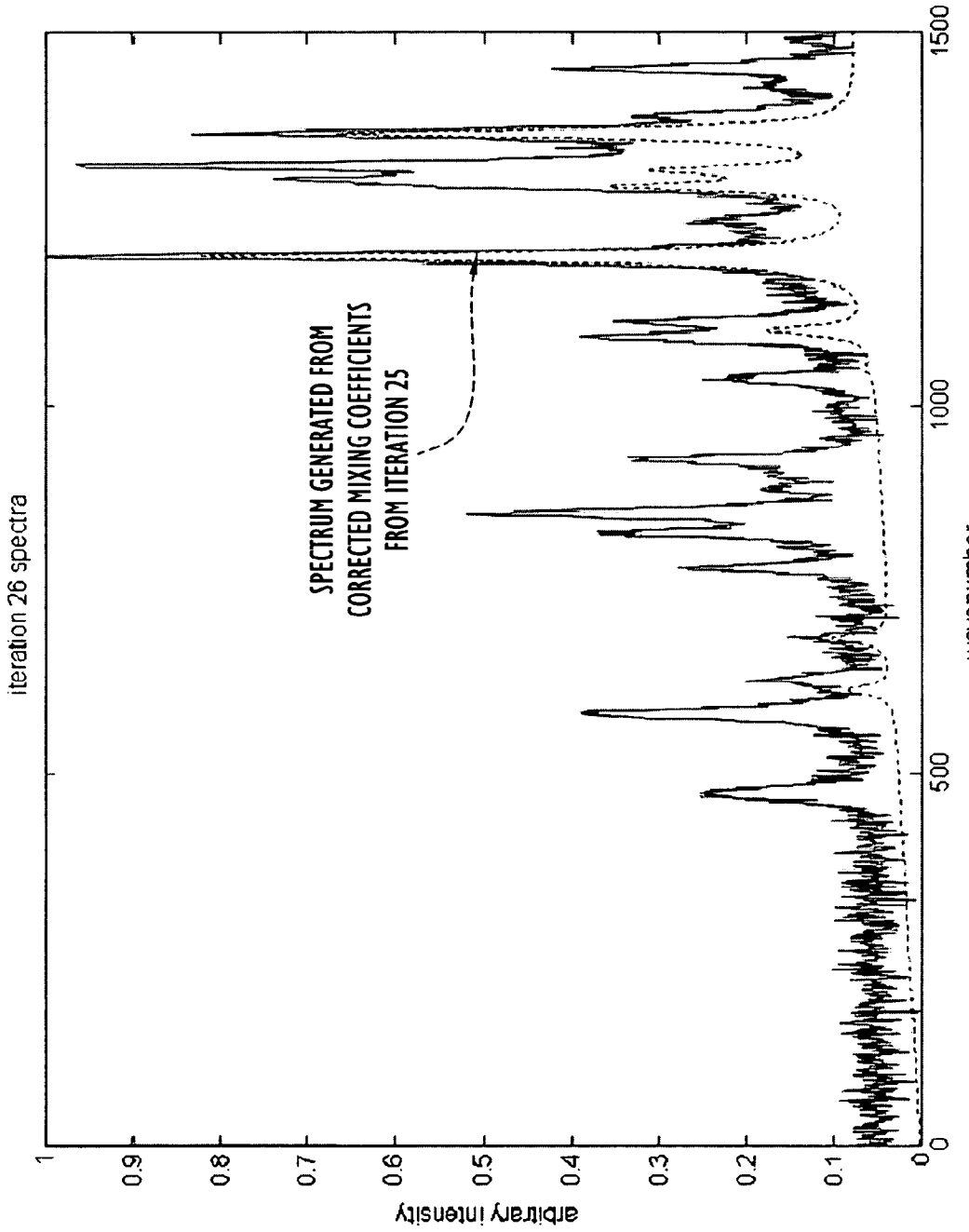

iteration 26 spectra
SPECTRUM GENERATED FROM
CORRECTED MIXING COEFFICIENTS
FROM ITERATION 25
arbitrary intensity
wavenumber
0
0.1
0.2
0.3
0.4
0.5
0.6
0.7
0.8
0.9
1
0
500
1000
1500

FIG.9A

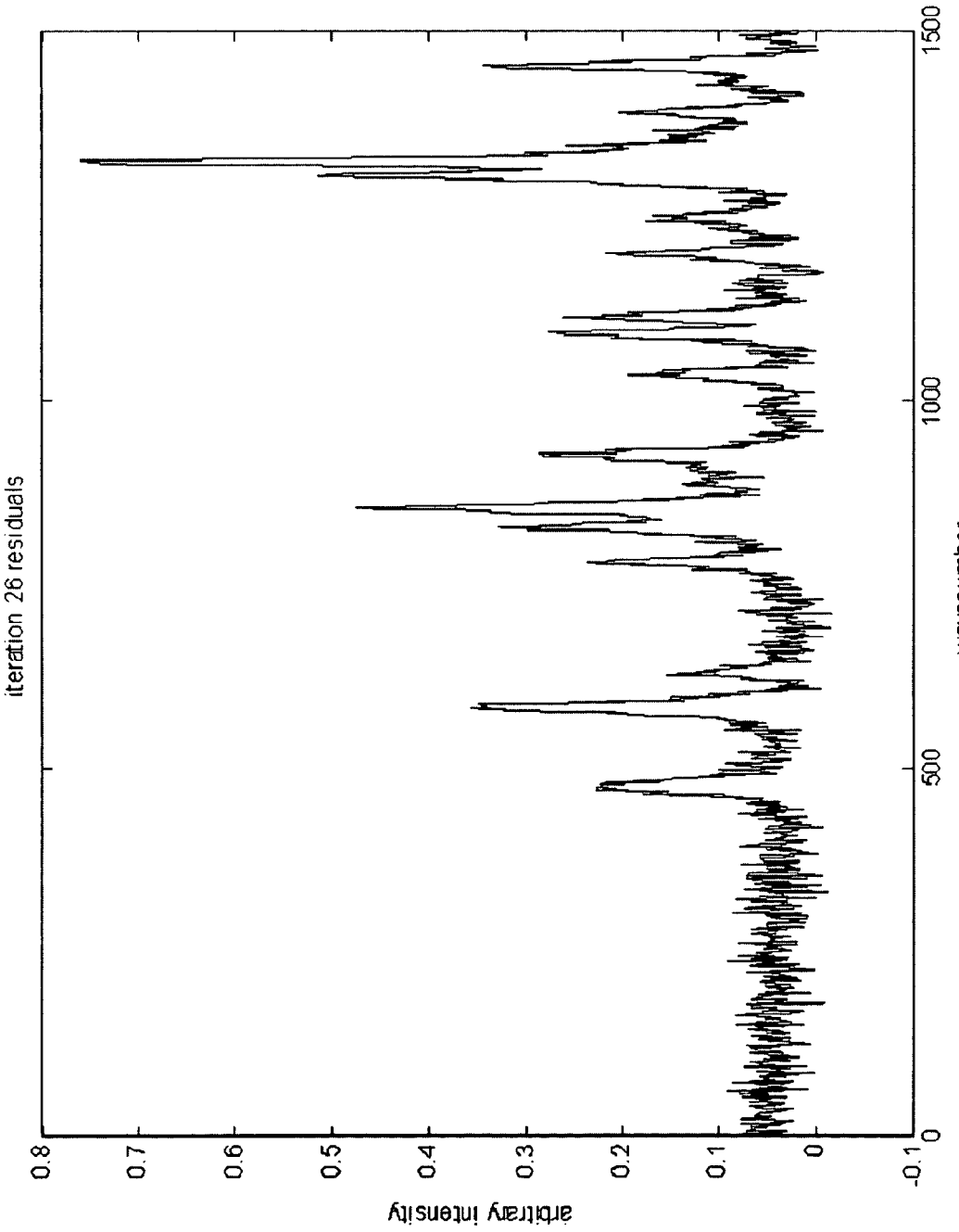

iteration 26 residuals
arbitrary intensity
wavenumber
0.8
0.7
0.6
0.5
0.4
0.3
0.2
0.1
0
-0.1
0
500
1000
1500

FIG.9B

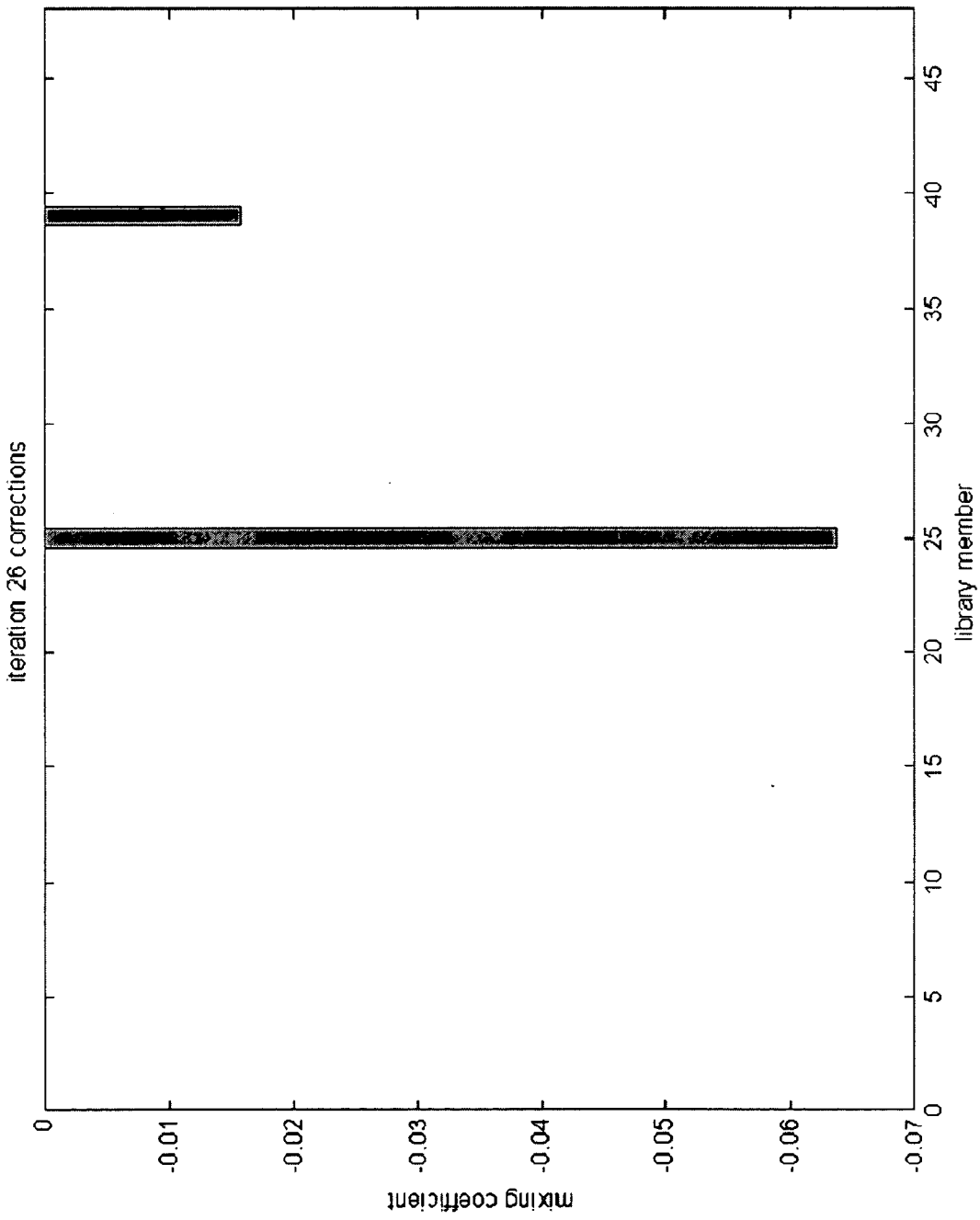

iteration 26 corrections
mixing coefficient
0
-0.01
-0.02
-0.03
-0.04
-0.05
-0.06
-0.07
0
5
10
15
20
25
30
35
40
45
library member

FIG.9C

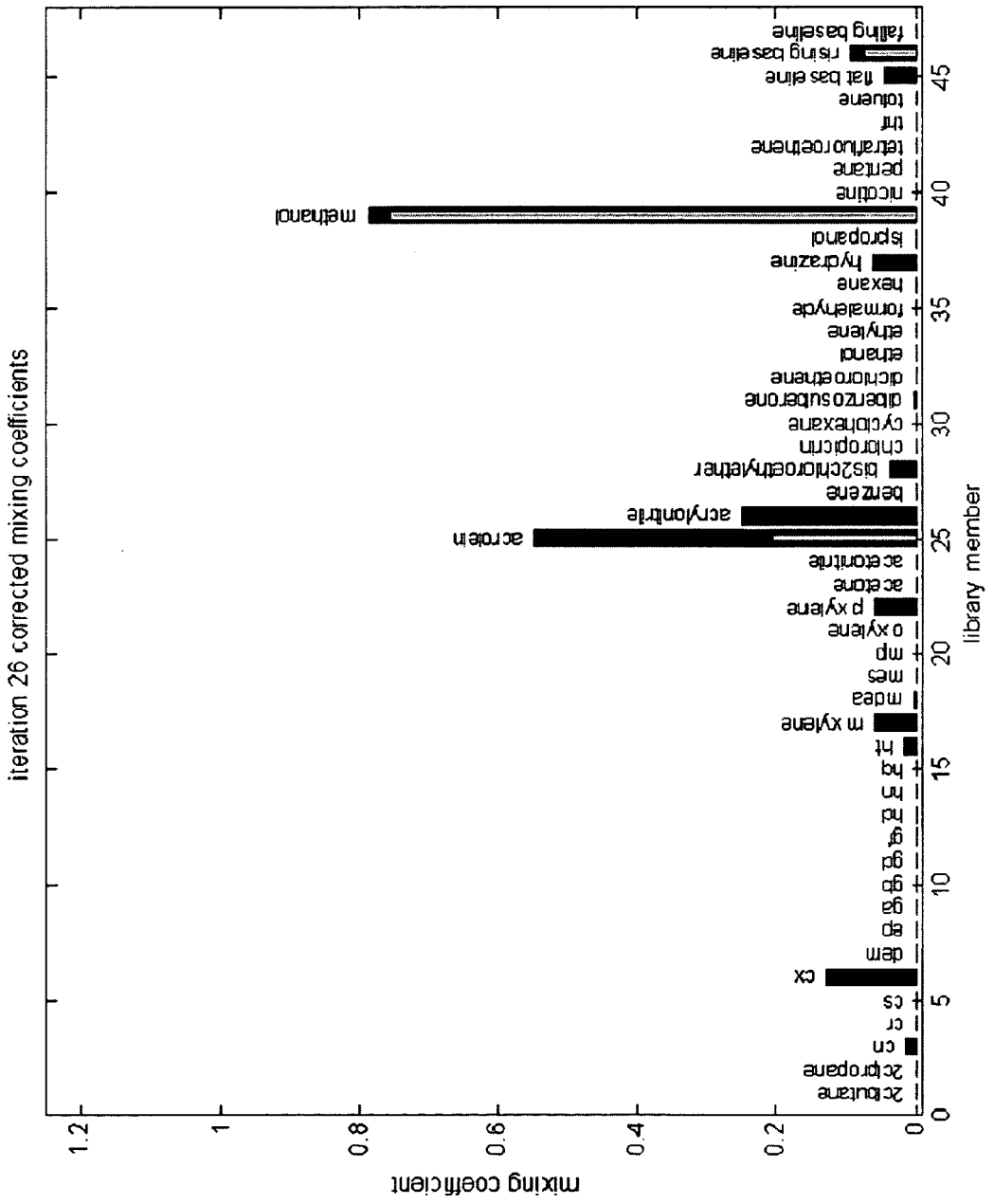

iteration 26 corrected mixing coefficients
mixing coefficient
library member
2c4butane
2c3propane
cn
cr
cs
cx
dem
ep
g3e
g3b
g4d
hfc
hn
hq
ht
m xylene
mdea
mes
mp
o xylene
p xylene
acetone
acetonitrile
acrolein
acrylonitrile
benzene
bis2chloroethylether
chloropicrin
cyclohexane
dibenzosuberone
dichloroethene
ethanol
ethylene
formaldehyde
hexane
hydrazine
isopropanol
methanol
nicotine
pentane
tetrachloroethene
thf
toluene
flat baseline
rising baseline
falling baseline

FIG.9D

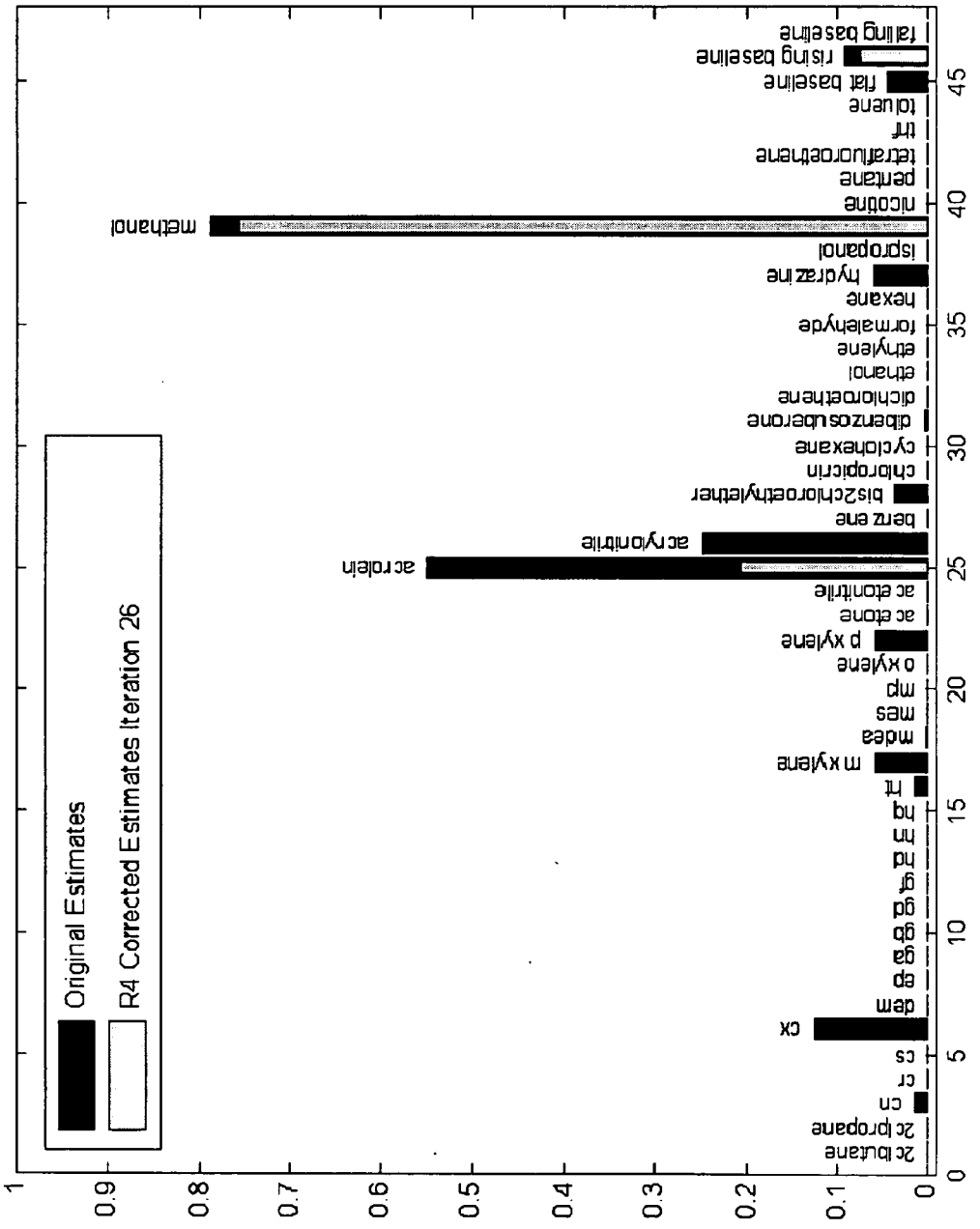

Original Estimates
R4 Corrected Estimates Iteration 26
2c butane
2c propane
cn
cr
cs
cx
dem
ep
ga
gb
gd
gg
hd
hn
hq
ht
m xylene
mdea
mes
mp
o xylene
p xylene
ace tone
ac etonitrile
acrolein
acrylonitrile
benz ene
bis2chloroethylether
chloropicrin
cyclohexane
dibenzosuberone
dichloroethene
ethanol
ethylene
formaldehyde
hexane
hydraz ine
isopropanol
methanol
nicotine
pentane
tetrafluoroethene
thf
toluene
flat baseline
rising baseline
falling baseline
0
0.1
0.2
0.3
0.4
0.5
0.6
0.7
0.8
0.9
1
0
5
10
15
20
25
30
35
40
45

FIG.10

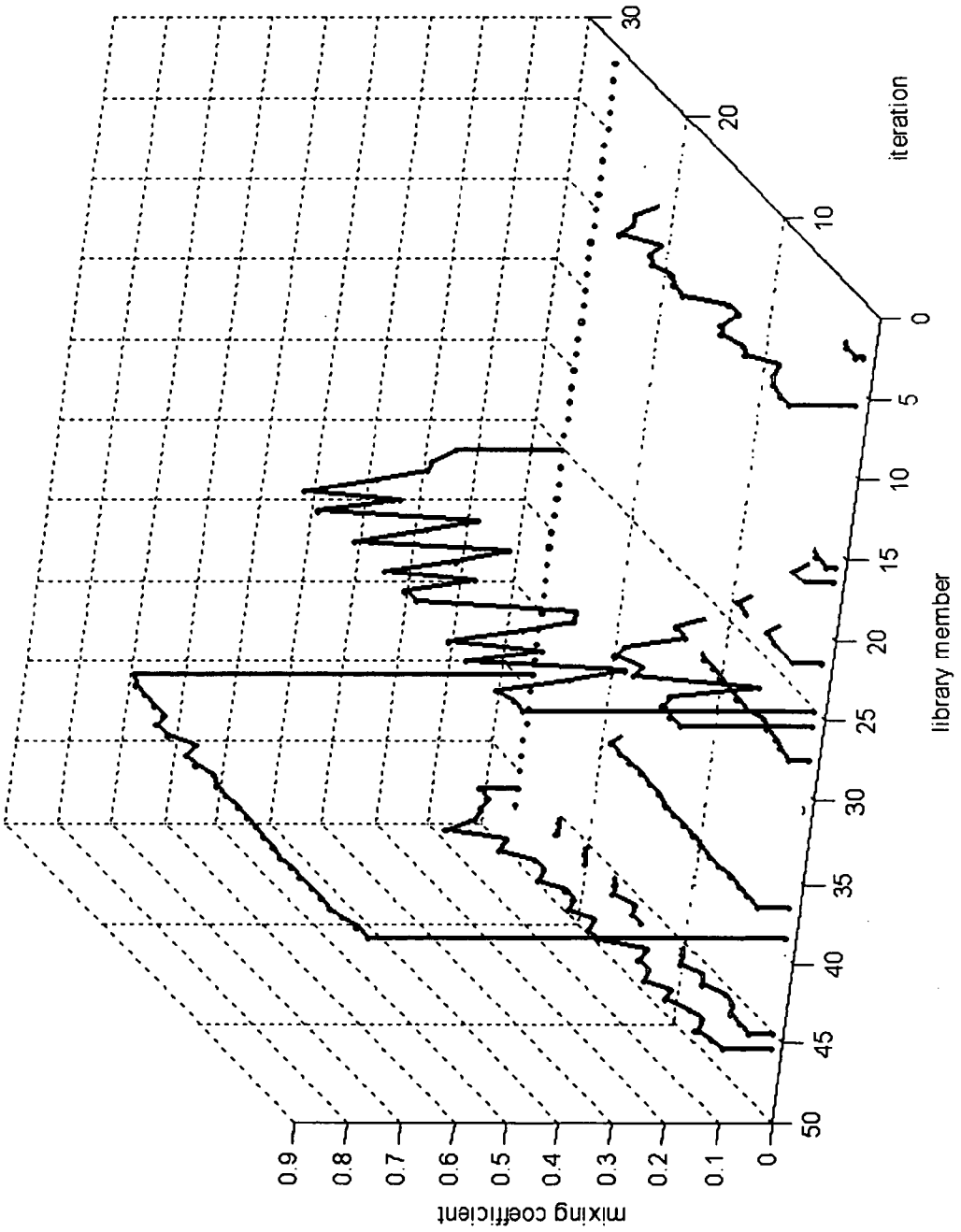

mixing coefficient
0.9
0.8
0.7
0.6
0.5
0.4
0.3
0.2
0.1
0
library member
0
5
10
15
20
25
30
35
40
45
50
iteration
0
10
20
30

FIG.11

RETRO-REGRESSION RESIDUAL REMEDIATION FOR SPECTRAL/SIGNAL IDENTIFICATION

BACKGROUND OF THE INVENTION

[0001] The present invention is directed to a method for improving performance of spectroscopic algorithms that are used to classify spectra, and more particularly to techniques to make spectroscopic algorithms more robust when analyzing data from unknown constituents.

[0002] Spectroscopy is a key technology for remote detection of biological or chemical constituents (such as biological and chemical warfare agents). The common thread in all spectroscopies is that each chemical and/or biological substance has a unique spectrum due to their unique structure. One of the goals of qualitative spectroscopy is to determine the component makeup of a substance given a library of the spectra of pure compounds. Quantitative analysis is not always necessary, and based on the sensor's construction and its operation, may not be possible. The use of spectroscopy requires algorithms that are capable of classification and de-convolution of spectra that arise from mixed substances. Regression methods are commonly used for qualitative data analysis. Multiple Linear Regression (MLR) methods are extremely useful for classification and deconvolution of mixed signals with a set of known library signals, called library spectra. Operationally, a library of spectra and a measured spectrum are input into the MLR model. The output is a vector called "mixing coefficients" that describes the quantities of the library spectra needed to linearly add the library spectra thereby generating a "best-fit" spectrum that is sufficiently close to the measured spectrum. Calculation of the mixing coefficients varies by model, and constraints may be employed. The advantages of MLR models for mixed signal identification include simplicity of implementation and operation, simultaneous determination of multiple compounds, speed of operation and the ability to use "pure" library spectrum (rather than a population of spectra to span the error space). In addition, most MLR models are based on rules that are consistent with the physics of spectroscopy in general. One particular advantage of many simple MLR models, including Classical Least Squares (CLS), is that no assumptions about the underlying probability densities of the signals need to be made or determined a priori. The importance of the contemporary algorithms cannot be overstated as these techniques are at the forefront of unmanned chemical and biological warfare detection.

[0003] These contemporary algorithms perform well against known compounds that are represented in the spectral library but are limited in their ability to handle unknown constituents that are not present in the library. Typically such unknowns will cause false alarms, as the algorithms attempt to use the library to describe the spectral features introduced by the unknowns. Historically, unknown spectral constituents are the Achilles heel of spectroscopic analysis. When performing spectroscopy in an uncontrolled setting (e.g., remote spectroscopic sensing of the environment) the assumption that the library contains everything that might generate a spectroscopic response is violated. At the onset, this puts conventional algorithms at a disadvantage, due to their inability to compensate for unknowns. Furthermore, many unknowns may share spectral similarity with any number of chemicals in the library, which further exacerbates the false alarm problem. For example, the functional group phosphate is responsible for a characteristic Raman peak in many chemical warfare agents such as Sarin, Soman, and Tabun. Similar chemical structure and therefore similar spectral features may be found in many of the pesticides sold in retail gardening stores. Unknown signals are ubiquitous and frequently degrade the sensor's performance even on well characterized signals. Thus, when unknowns are present, they tend to cause false positive detections. This introduces type II errors (accepting a false hypothesis).

[0004] Due to the almost infinite number of substances that may be encountered, it is impossible to include every possible constituent in the library spectra. This leaves the qualitative spectroscopist with three choices:

[0005] 1. Ignore the unknowns and hope that they do not affect the analysis.

[0006] 2. Control the sample rigorously—this may mean that samples are pre-treated to separate out anything besides the items of interest.

[0007] 3. Build algorithms and routines that are robust against unknowns.

[0008] The first choice is the most common solution: make the a priori assumption that unknowns will not be present or if they are present, they will not cause significant problems. Although this greatly simplifies the problem of identification, for real world applications, those are dangerous assumptions to make. For these reasons, the second choice is often used in industrial settings, laboratory settings, and in environmental testing, where it is convenient to obtain a sample and perform the wet chemistry or preparative separation on it prior to (and sometimes in conjunction with) spectroscopic analysis. Pre-treatment is not always the most desirable choice, especially if the samples being analyzed are dangerous or if the samples are being sensed at such a distance, frequency, or under other circumstances that make pre-treating impossible. Thus, the better solution for performing real-time or in-the field measurements of un-treated samples is to make algorithms and routines robust to unknowns.

[0009] Attempts have been made to overcome these problems by either adding the unknown features into a calibration library, or subtracting them from the sample. All of these techniques involve analysis of quantitative data, and seek to correct both for unknowns and for disturbances in the spectrum due to disparate environmental effects. These methods require extensive knowledge of the system being measured, which is not available when performing remote analysis of environmental samples, in which the sensor may contain some variance, and the samples analyzed are unconstrained with respect to chemical composition. Another disadvantage for these competing attempts is that they require expert knowledge, and frequently expert operation, which hinders the ability of the algorithm to work unassisted, as a remote, real-time system would need to.

[0010] What is needed is a technique for automatically correcting spectroscopic analysis for unknown components present in the measured mixture.

SUMMARY OF THE INVENTION

[0011] Briefly, a system and method are provided for improving regression-based qualitative analysis when the

mixture to be analyzed contains a compound not in the library spectra, a so-called unknown. A regression of a measured spectrum taken of a sample is computed against the library spectra. This regression is referred to as a "master" regression. Estimated mixing coefficients of the sample are computed from the regression. Next, a vector of residual error is computed using the "best-fit" spectrum (generated using the library and the estimated mixing coefficients) and the measured spectrum. Peaks in the residual error are identified that extend in a direction opposite to that of peaks in the measured spectrum. These peaks are referred to as "negative" peaks. A regression is performed on the "negative" peaks with the library. This is referred to as a "retro-regression," to be distinguished from the master regression performed on the measured spectrum. The mixing coefficients generated in the retro-regression are used to compensate for overprediction in previous steps. Using the retro-regression mixing coefficients, corrected mixing coefficients are computed. This process repeats where the corrected mixing coefficients replace the estimated mixing coefficients for a new estimated spectrum that is used to compute a new residual error.

[0012] Furthermore, the corrected mixing coefficients may be examined to determine whether there is a member of the library whose mixing coefficient is less than a threshold. If so, that member is removed from the library spectra and a new master regression is computed without that library member. The new estimated mixing coefficients are used for computing the residual error at the next iteration.

[0013] Termination of the process may occur when there are no more negative peaks in the residuals, there are no more members in the library spectra, or a maximum number of iterations are reached.

[0014] This retro-regression remediation technique makes MLR algorithms more robust to unknowns. Used in conjunction with MLR techniques, estimates are generated in a manner that utilizes the error structure which arises from the constraints of spectroscopy to eliminate false alarms. Furthermore, this approach allows for improved analysis of the unknown constituents. The known compounds may be identified, and removed, storing the best-unknown spectrum for further "forensic" chemical analysis on it at a later date. No knowledge is assumed about the composition of the sample. This algorithm works with minimum user input. It is as an add-on to other regression techniques (i.e. Classical Least Squares) to eliminate false positive errors. However, the techniques described herein may be generalized to improve performance of any other regression model that follows the basic assumptions of optical spectroscopy.

[0015] The above and other objects and advantages will be more readily apparent when reference is made to the following description taken in conjunction with the accompanying drawings.

BRIEF DESCRIPTION OF THE DRAWINGS

[0016] **FIG. 1** is a block diagram of a spectroscopic analysis system.

[0017] **FIG. 2** is general flow chart of a spectroscopic analysis process.

[0018] **FIG. 3** is a flow chart depicting steps of the spectroscopic analysis process employing the retro-regression residual remediation algorithm.

[0019] **FIG. 4** lists the members of the library spectra for an example described herein.

[0020] **FIG. 5A** is a plot showing a measured spectrum taken from a sample and the estimated or best-fit spectrum generated from the master regression coefficients.

[0021] **FIG. 5B** is a chart showing the mixing coefficients generated from the master regression computation.

[0022] **FIG. 5C** is a plot showing the residual error between the measured spectrum and the best-fit estimated spectrum shown in **FIG. 5A**.

[0023] **FIG. 6A** is a chart showing the retro-regression coefficients computed in iteration **1** from the residuals shown in **FIG. 5B**.

[0024] **FIG. 6B** is a chart showing the corrected mixing coefficients for iteration **1** computed from the retro-regression coefficients shown in **FIG. 6A**.

[0025] **FIG. 7A** is a plot showing the measured spectrum and an estimated spectrum at iteration **2** that is generated from the corrected mixing coefficients from iteration **1**.

[0026] **FIG. 7B** is a plot showing the residual error between the measured spectrum and the estimated spectrum shown in **FIG. 7A** for iteration **2**.

[0027] **FIG. 7C** is a chart showing the retro-regression coefficients computed in iteration **2** from the residuals shown in **FIG. 7B**.

[0028] **FIG. 7D** is a chart showing the corrected mixing coefficients for iteration **2** computed from the retro-regression coefficients shown in **FIG. 7C**.

[0029] **FIG. 8A** is a plot showing the measured spectrum and an estimated spectrum at iteration **25** that is generated from the corrected mixing coefficients from iteration **24**.

[0030] **FIG. 8B** is a plot showing the residual error between the measured spectrum and the estimated spectrum shown in **FIG. 8A** for iteration **25**.

[0031] **FIG. 8C** is a chart showing the retro-regression coefficients computed in iteration **25** from the residuals shown in **FIG. 8B**.

[0032] **FIG. 8D** is a chart showing the corrected mixing coefficients for iteration **25** computed from the retro-regression coefficients shown in **FIG. 8C**.

[0033] **FIG. 9A** is a plot showing the measured spectrum and an estimated spectrum at iteration **26** that is generated from the corrected mixing coefficients from iteration **25**.

[0034] **FIG. 9B** is a plot showing the residual error between the measured spectrum and the estimated spectrum shown in **FIG. 9A** for iteration **26**.

[0035] **FIG. 9C** is a chart showing the retro-regression coefficients computed in iteration **26** from the residuals shown in **FIG. 9B**.

[0036] **FIG. 9D** is a chart showing the corrected mixing coefficients for iteration **26** computed from the retro-regression coefficients shown in **FIG. 9C**.

[0037] **FIG. 10** is a plot showing a comparison of the corrected mixing coefficients generated using the retro-

regression remediation techniques and the mixing coefficients generated without the retro-regression remediation techniques.

[0038] **FIG. 11** is a plot showing how library members are removed from the library spectra in the retro-regression remediation process as their mixing coefficients fall below a threshold.

DETAILED DESCRIPTION

[0039] Referring first to **FIG. 1**, a spectroscopic analysis system **10** is shown comprising a sensor **100** coupled to a processor **120**. Memory **130** is provided that stores the software that performs the analysis algorithm **140** and a library **150** that contains spectrum data associated with numerous chemicals against which the analysis algorithm **140** operates. The sensor **100** scans or otherwise performs a spectroscopic measurement on a mixture **110** to be analyzed. The mixture **110** may be a solid, liquid or gas substance.

[0040] As shown in **FIG. 2**, the spectroscopic analysis process involves executing the analysis algorithm **100** on the measured spectrum data produced by the sensor against the library spectra. The outputs of the analysis algorithm are qualitative spectrum analysis results on the mixture.

[0041] Certain assumptions are made when utilizing current spectroscopic analysis algorithms, and when these assumptions are met everything works well and the algorithm provides reliable results. The assumptions include linearity, linear additivity, all pure spectra known, uniqueness, and non-negativity of physical quantities. However, when performing remote sensing, the all pure spectra known assumption is frequently violated, causing problems with how these algorithms handle unknowns. The typical result is an overestimation of "library" chemicals, often resulting in false positive alarms (Type II errors).

[0042] Assumptions may be made regarding error structures arising from regression-based techniques applied to spectroscopic data. Since a substance may either be present in a certain quantity, or is absent, concentration quantities have a minimum of zero. Unlike with time based signals such as radar, there is no signal-based interference such as phase mixing. For this reason, in conventional spectroscopy spectra may always add together, but will never cancel each other out, and therefore are never assigned negative concentration/intensity values in the absence of specific data pre-processing techniques not employed herein. Using these assumptions, the algorithm described herein functions as an add-on to other regression techniques that would eliminate false positive errors. If the residual error is defined as the modeled signal subtracted from the original signal (spectrum) and the signal is one that extends in the positive direction, then errors that extend in the positive direction are portions of the original spectrum that are poorly modeled (i.e., an unknown spectrum or portions thereof) and errors in the negative direction are indicators that library spectra members are being erroneously used to model an unknown. Identification of the spectra causing the negative residuals, and removal of those spectra from the library will eliminate the major source of false positives in regression based classification models. This algorithm is referred to as a retro-regression residual removal ("R4") algorithm.

[0043] The R4 algorithm may be an add-on to Multiple Linear Regression (MLR) type regression models that follow the basic assumptions of optical spectroscopy. It has the following benefits:

[0044] 1. Eliminates of false alarms,

[0045] 2. Operates in the presence of unknown constituents,

[0046] 3. Improves quantitative accuracy (when desired),

[0047] Theory of R4

[0048] When using Classical Least Squares (CLS) for multiple component identification or quantification, the inherent assumptions made are:

[0049] Linearity: The relationship between the intensity of the signal vector and its concentration (i.e. quantity) is linear over the range measured.

[0050] Linear additivity: The signal response to a mixture is the same as if the signals were collected separately and added together subsequent to collection.

[0051] All pure spectra known: The constituents of the mixture are all present in the library of signals.

[0052] Uniqueness/Non-Singularity: The library signals all have some degree of uniqueness, even if there are certain similar features between signals in the library, and none of the signals may be added such that the result is collinear with any other signal.

[0053] Non-Negativity: Although not a mathematical requirement, frequently the concentration or quantity values are constrained to non-negative estimates because negative values have no physical meaning when quantities of material are concerned.

[0054] The signals and quantities of interest include:

[0055] r unknown signal;

[0056] S=library of pure signals; and

[0057] c=concentrations or relative amounts of each signal in S

[0058] In the MLR model, if all of the assumptions hold, it may be stated that

$$r=cS$$

and that S and r may be used to generate an estimate of c, ĉ, in the following manner

$$rS^{+}=\hat{c}$$

where ĉ is an estimate of c, whose fidelity is based on the completeness and accuracy of S, any error in the system, the computation of the pseudo-inverse of S, S^{+}, and the compliance with the assumptions of MLR. The (unknown) signal of interest may be reconstructed using ĉ and S.

$$\hat{r}=\hat{c}S$$

[0059] The fidelity of this reconstruction, r̂, depends on the factors listed above. A vector of residual errors, ϵ may be generated by looking at the difference between r and r̂.

$$\epsilon=r-\hat{r}$$

[0060] If all of the assumptions hold, the vector of residual errors ϵ should be the random noise in the system, and tends not to be intrinsically useful or interesting. However, if the

assumptions are violated, the residual error vector ϵ contains information that is useful in determining the source of the violations.

[0061] If the errors are computed in the manner described above, the errors could be described as coming from three sources. The first source is the signal that arises from noise in the instrument. This tends to be random and uninteresting for the sake of this analysis. The second source is the spectrum of peaks that were in the measured spectrum that are not fit by the library members. Peaks in this direction are typically indicative of under-predicted peaks which are caused either by the presence of an unknown, or by under-prediction of known substances. The third source of error is due to over-prediction (and often mis-prediction) which occurs when library spectra are used to try to fit unknowns. The error caused by these peaks extends in the direction opposite to that of the original peaks in the measured spectrum.

[0062] Depending on the type of spectroscopy, peaks are portrayed in many ways. In emissive-type spectroscopy (Raman, Fluorescence, Mass Spectrometry) peaks extend upward from some baseline. In absorbance-type spectroscopy (Active NIR, UV-Vis absorbance) the peaks extend down from some baseline or theoretical absolute (e.g., 100% transmission). Both of these types of spectroscopy could be deemed monotonic, since when peaks are observed, the peaks extend in only one direction. This is contrasted with passive IR which has peaks that extend in both directions. Therefore, when negative residuals are mentioned, the intention is to describe peaks that extend in the direction opposite to the normal extension of the peaks.

[0063] Referring to **FIG. 3**, the R4 process **300** will be described. In step **302**, a mixture to be analyzed is scanned or monitored in order to collect measured spectrum data. Next, in step **310**, any baseline effects in the measured spectrum are identified and removed. Baseline effects, such as CCD dark current, fluorescence in the case of Raman Spectroscopy, or non-coherent scattering in the case of NIR spectroscopy are phenomena which will introduce some bias into the spectra. In order to determine the direction of the residuals relative to the original signal, this baseline must be identified. In step **320**, the peak direction in the measured spectrum is identified with respect to the baseline. For example, it is determined whether the peaks in the measured spectrum are positive or negative with respect to the baseline. Next, in step **330**, a "master" regression is performed on the measured spectrum against the library spectra. For example, an MLR regression may be used in step **330**. In step **340**, initial estimated (or best-fit) mixing coefficients are computed of the sample from the master regression. An estimated or "best-fit" spectrum is generated using the library and the estimated mixing coefficients.

[0064] A loop is defined by steps **350** through **364** during which corrected mixing coefficients are computed using a "retro-regression" computation. The corrected mixing coefficients produced at the completion of an iteration through the loop replace the estimated mixing coefficients computed in step **350** for purposes of computing a new residual error. Loop control step **364** tests whether certain criteria are met to stop iterating through the loop, and if none of these criteria is met, another iteration is made through the loop.

[0065] More specifically, in step **350**, the residual error between the estimated spectrum and the measured spectrum is computed by subtracting the estimated spectrum from the measured spectrum. The residual error is also referred to herein as the "residuals". The first time into the loop (iteration **0**), the estimated spectrum is the best-fit spectrum computed in step **340**. In step **352**, peaks are identified that extend in a direction opposite from the peaks in the measured spectrum. These peaks may be referred to as "negative" peaks, but it should be understood that they may extend in a positive direction if the peaks in the measured spectrum extend in a negative direction. Next, in step **354**, the negative peaks are isolated. Then, in step **356**, a "retro-regression" computation is performed. For example, the same regression method that was used to compute the master regression is used to compute the retro-regressions in order to remove specific deleterious effects that the master regression introduced. That is, the negative peaks are regressed against the library spectra to produce corrections to the originally over-predicted master mixing coefficients. In step **358**, the retro-regression coefficients computed in step **356** are used to compute corrected mixing coefficients by subtracting the retro-regression mixing coefficients from the estimated mixing coefficients computed at the prior iteration, or if the first iteration, then the mixing coefficients generated from the master regression in step **340**. This corrects the master regression concentration estimates computed during the first iteration.

[0066] Next, in step **360**, any member in the library whose estimate in the corrected mixing coefficients is less than a threshold (typically the precision of the computer: 10^{-16}) is removed. And in step **362**, if a library member is removed in step **360**, then the master regression (already once performed in step **330**) is re-computed for the measured spectrum against the (new) library that now does not include the library member(s) removed in step **360**. New (estimated) mixing coefficients are consequently computed in step **362** and used in the subsequent steps in place of the corrected mixing coefficients computed at the prior iteration for purposes of computing the residual error in step **350**.

[0067] In the loop control step **364**, a determination is made whether there are no more members of the library (as a result of the removal in step **360**), no more negative peaks remain or a maximum number of iterations have been reached. If any of these criteria are met in step **364**, the process **300** terminates and the estimated mixing coefficients computed up to this point represents the final mixing coefficients of the analysis. Otherwise, steps **350** through **364** are repeated where the corrected mixing coefficients computed in step **358** (or the new estimated mixing coefficients computed in step **362**) replace the estimated mixing coefficients from the prior iteration that are used to generate the estimated spectrum for the next iteration through the steps **350** through **364**. An example of a maximum number of iterations is 100. An example of a "no more negative" peaks situation is when there are no regions at least five (5) contiguous points. Five or more contiguous negative residual points may be referred to as a contiguous block. Five is an arbitrarily selected value, and may be changed based on the resolution and noise characteristics of the system on which the R4 algorithm is applied.

[0068] Many of the computations in various steps of the process **300** may be performed using techniques known in the art. For example, "peak picker" routines are known to identify peaks in a signal. In step **352**, negative peaks using

the criterion explained above of a certain number (e.g., five) of negative (or positive if the original measured spectrum is negative) contiguous points. To say it more generally, a peak is identified as at least a predetermined number of contiguous points that are on the opposite side, with respect to a baseline, to peaks in the measured spectrum. The "negative" nature of a point may be based on area in a negative direction, length in a negative direction and/or angle relative to peaks in the measured spectrum.

[0069] Turning to **FIGS. 4-11**, with continued reference to **FIG. 3**, data produced at various points of the process **300** will be described to illustrate how the process **300** operates for a simulation example. **FIG. 4** shows lists the names of the compounds that are members in the exemplary library. In this simulation example, the unknown substance is Carbaryl. That is, Carbaryl is not in the library spectra. A spectrum was generated by simulating a spectrum of Carbaryl, normalizing it, multiplying it by 0.5, adding it to a normalized spectrum of methanol (a member of the library spectra). The simulation was done to demonstrate the ability of the process **300** to reduce and/or reject predictions of anything except methanol.

[0070] Iteration **0**

[0071] **FIG. 5A** shows the measured spectrum (dashed line) and the initial estimated or best-fit spectrum (solid line) generated from the master regression coefficients computed in step **330**. **FIG. 5B** shows the mixing coefficients generated from the master regression computation of step **330**. **FIG. 5C** shows the residual error between the measured spectrum and the best-fit spectrum shown in **FIG. 5A**.

[0072] Iteration **1**

[0073] **FIG. 6A** shows the retro-regression coefficients computed in step **356** computed by performing a regression on the negative peaks identified in the residuals shown in **FIG. 5C**. **FIG. 6B** is a chart showing the corrected mixing coefficients computed from the retro-regression coefficients shown in **FIG. 6A** and from the master regression coefficients shown in **FIG. 5B**.

[0074] Iteration **2**

[0075] **FIG. 7A** is a plot showing the measured spectrum and an estimated spectrum computed from the corrected mixing coefficients shown in **FIG. 6B**. **FIG. 7B** is a plot showing the residuals computed for the estimated spectrum shown in **FIG. 7A**. **FIG. 7C** is a chart showing the retro-regression coefficients computed for the negative peaks identified in the residuals shown in **FIG. 7B**. **FIG. 7D** is a chart showing the corrected mixing coefficients computed from the retro-regression coefficients shown in **FIG. 7C** and the corrected mixing coefficient shown in **FIG. 6B** for the prior iteration.

[0076] This process repeats for several iterations as described above. At the next iteration, residuals are computed from the new mixing coefficients computed in step **362** or the corrected mixing coefficients computed in **358** from the prior iteration. Then the negative peaks are identified and isolated and a retro-regression is computed on the negative peaks. The corrected mixing coefficients are then computed by subtracting the retro-regression coefficients from the estimated mixing coefficients from the prior iteration. In this example, the process terminates after the 26th iteration for reasons explained below.

[0077] Iteration **25**

[0078] **FIG. 8A** shows the plots for the measured spectrum and an estimated spectrum generated from the corrected mixing coefficients computed at iteration **24** (not shown). **FIG. 8B** shows the residuals computed using the estimated spectrum shown in **FIG. 8A**. **FIG. 8C** shows the retro-regression coefficients computed from the one remaining negative peak of the residuals shown in **FIG. 8B**. **FIG. 8D** is a chart showing the corrected mixing coefficients computed from the retro-regression coefficients shown in **FIG. 8C** and the corrected mixing coefficients at iteration **24** (not shown).

[0079] Iteration **26**

[0080] **FIG. 9A** shows the measured spectrum and an estimated spectrum generated from the corrected mixing coefficients shown in **FIG. 8D**. **FIG. 9B** shows the residuals computed using the estimated spectrum shown in **FIG. 9A**. **FIG. 9C** is a chart showing the retro-regression coefficients computed from the negative peaks of the residuals shown in **FIG. 9D**. Notice that there are no negative peaks in the residuals shown in **FIG. 9C**. **FIG. 9D** shows the corrected mixing coefficients computed from the retro-regression coefficients shown in **FIG. 9C** and the corrected mixing coefficients shown in **FIG. 8D**. Because there are no negative peaks in the residuals at the 26^{th} iteration, the process now terminates.

[0081] Explanation of Simulation Results

[0082] **FIG. 10** shows the original mixing coefficients computed at the master regression step **330** and the corrected mixing coefficients at the 26^{th} iteration.

[0083] This figure essentially compares the performance of the R4 algorithm with a standard CLS algorithm used to analyze a mixture that has a compound that is not in the library spectra. Due to the peaks of Carbaryl, the unknown, several other chemicals, namely Acrolein, Acrylonitrile, and CX, are falsely identified as being present using a CLS algorithm, some at fairly high amounts. However, using the retro-regression remediation techniques described herein, the false positives of standard CLS are removed, and do not appear in the resulting mixing coefficients to any significant degree. Methanol appears in the corrected mixing coefficients, as it should, because it was present in the measured spectrum and is part of the library spectra. While Acrolein still appears in the corrected mixing coefficients, it is in substantially lower amounts than without the retro-regression techniques. Its amount is so low that it would not trigger a false positive identification.

[0084] The R4 algorithm removes the residuals that are due to miss-identification of library members not present in the unknown spectrum. Upon complete removal of a library member a complete recalculation of the "master" mixing coefficients is performed. This re-computation is performed because upon removal of a library member, the mixing coefficients may change. Thus, re-calculation is performed to yield a more accurate assessment of the composition of the sample. In the example data, it may be seen that performing the re-calculation upon removal of a library member does add extra computations and extends the time

required to iterate, but in the end superior rejection of spurious spectra is achieved. At each re-calculation the mixings are inflated, and the R4 algorithm works to reduce them.

[0085] **FIG. 11** shows that several members of the library are removed over the retro-regression iterations (step **260** in **FIG. 3**). Upon termination, the coefficients are strong only for the true remaining members of the library.

[0086] To summarize, a method for improving regression-based spectroscopic analysis, comprising: (a) computing a residual error between an estimated spectrum and a measured spectrum taken of a sample, wherein the estimated spectrum is derived from mixing coefficients for members of a library of spectra that are produced by computing a regression on the measured spectrum with the library; (b) identifying peaks in the residual error that extend in a direction opposite to that of peaks in the measured spectrum; (c) performing a regression on the peaks to produce retro-regression coefficients; (d) computing corrected mixing coefficients based on the retro-regression coefficients; and (e) repeating (a) through (d) with the corrected mixing coefficients computed in (d) being used to generate a new estimated spectrum for computing the residual error in (a) at the next iteration.

[0087] Similarly, a processor readable medium is provided storing instructions that, when executed by a processor, cause the processor to: (a) compute a residual error between an estimated spectrum and a measured spectrum taken of a sample, wherein the estimated spectrum is derived from a mixing coefficients for members of a library of spectra that are produced by computing a regression on the measured spectrum with the library; (b) identify peaks in the residual error that extend in a direction opposite to that of peaks in the measured spectrum; (c) perform a regression on the peaks to produce retro-regression coefficients; (d) compute corrected mixing coefficients based on the retro-regression coefficients; and repeat (a) through (d) with the corrected mixing coefficients computed in (d) being used to generate a new estimated spectrum for computing the residual error in (a) at the next iteration.

[0088] In addition, a system for spectroscopic analysis comprising: a sensor that produces data from a mixture to be analyzed, and a processor coupled to the sensor, wherein the processor is programmed to: (i) generate a measured spectrum from the data produced by the sensor; (ii) perform a regression of the measured spectrum with a library of spectra; (iii) generate estimated mixing coefficients from the regression; (iv) compute a residual error between an estimated spectrum generated from the estimated mixing coefficients and the measured spectrum; (v) identify peaks in the residual error that extend in a direction opposite to that of peaks in the measured spectrum; (vi) perform a regression on the peaks to produce retro-regression coefficients; (vii) compute corrected mixing coefficients based on the retro-regression coefficients; and (viii) repeat (iv) through (vii) with the corrected mixing coefficients computed in (vii) being used to generate a new estimated spectrum for computing the residual error in (iv) at the next iteration.

[0089] Still further, a method is provided for processing spectroscopic measured data of a sample, comprising: (a) identifying peaks in a residual error between measured data and an estimated data computed from a regression performed on the measured data, wherein the peaks extend in a direction opposite to that of peaks in the measured data; (b) performing a regression on the peaks; (c) computing a corrected data based on the regression of the peaks; (d) computing a new residual error between the measured data and the corrected data; and (e) repeating (a) through (d) using the new residual error.

[0090] The system and methods described herein may be embodied in other specific forms without departing from the spirit or essential characteristics thereof. The foregoing embodiments are therefore to be considered in all respects illustrative and not meant to be limiting.

What is claimed is:

1. A method for improving regression-based spectroscopic analysis, comprising:

a. computing a residual error between an estimated spectrum and a measured spectrum taken of a sample, wherein the estimated spectrum is derived from mixing coefficients for members of a library of spectra that are produced by computing a regression on the measured spectrum with the library;

b. identifying peaks in the residual error that extend in a direction opposite to that of peaks in the measured spectrum;

c. performing a regression on the peaks to produce retro-regression coefficients;

d. computing corrected mixing coefficients based on the retro-regression coefficients; and

e. repeating (a) through (d) with the corrected mixing coefficients computed in (d) being used to generate a new estimated spectrum for computing the residual error in (a) at the next iteration.

2. The method of claim 1, and further comprising (f)(1) removing a member of the library whose mixing coefficient in the corrected mixing coefficients is less than a threshold.

3. The method of claim 2, wherein when a member of the library spectra is removed, further comprising (f)(2) performing a regression of the measured spectrum with the library without the member that was removed to produce new mixing coefficients, and wherein (e) of repeating comprises repeating (a) through (f)(2) the new mixing coefficients being used to generate a new estimated spectrum for computing the residual error at the next iteration.

4. The method of claim 3, wherein (e) repeating comprises repeating (a) through (f)(2) until no members of the library remain.

5. The method of claim 1, wherein (h) repeating comprises repeating (a) through (d) until there are no more peaks in the residual error.

6. The method of claim 1, wherein (b) identifying comprises identifying a peak as at least a predetermined number of contiguous points that are on the opposite side, with respect to a baseline, to peaks in the measured spectrum.

7. The method of claim 6, wherein (e) repeating comprises repeating (a) through (d) until there are no more regions in the residual error having at least the predetermined number of contiguous points.

8. The method of claim 1, wherein (d) computing corrected mixing coefficients comprises subtracting the retro-

regression coefficients from the mixing coefficients for the estimated spectrum used in computing the residual error in the current iteration.

9. A processor readable medium storing instructions that, when executed by a processor, cause the processor to:

a. compute a residual error between an estimated spectrum and a measured spectrum taken of a sample, wherein the estimated spectrum is derived from a mixing coefficients for members of a library of spectra that are produced by computing a regression on the measured spectrum with the library;

b. identify peaks in the residual error that extend in a direction opposite to that of peaks in the measured spectrum;

c. perform a regression on the peaks to produce retro-regression coefficients;

d. compute corrected mixing coefficients based on the retro-regression coefficients; and

e. repeat (a) through (d) with the corrected mixing coefficients computed in (d) being used to generate a new estimated spectrum for computing the residual error in (a) at the next iteration.

10. The processor readable medium of claim 9, and further comprising instructions stored on the medium that, when executed, cause the processor to (f)(1) remove a member of the library whose mixing coefficient in the corrected mixing coefficients is less than a threshold.

11. The processor readable medium of claim 10, and further comprising instructions stored on the medium that, when executed, cause the processor to (f)(2) perform a regression of the measured spectrum with the library without the member that was removed to produce new mixing coefficients, and that cause the processor to (e) repeat (a) through (f)(2) are repeated with the new mixing coefficients being used to generate a new estimated spectrum for computing the residual error at the next iteration.

12. The processor readable medium of claim 11, and further comprising instructions stored on the medium that, when executed, cause the processor to repeat (a) through (f)(2) until no members of the library remain.

13. The processor readable medium of claim 9, and further comprising instructions stored on the medium that, when executed, cause the processor to repeat (a) through (d) until there are no more peaks in the residual error.

14. The processor readable medium of claim 9, and further comprising instructions stored on the medium that, when executed, cause the processor to identify a peak as at least a predetermined number of contiguous points that are on the opposite side, with respect to a baseline, to peaks in the measured spectrum.

15. The processor readable medium of claim 9, and further comprising instructions stored on the medium that, when executed, cause the processor to repeat (a) through (d) until there are no more regions in the residual error having at least the predetermined number of contiguous points.

16. The processor readable medium of claim 9, and further comprising instructions stored on the medium that, when executed, cause the processor to (d) compute corrected mixing coefficients by subtracting the retro-regression coefficients from the mixing coefficients for the estimated spectrum used in computing the residual error in the current iteration.

17. A system for spectroscopic analysis comprising:

a. a sensor that produces data from a mixture to be analyzed; and

b. a processor coupled to the sensor, wherein the processor is programmed to:

i. generate a measured spectrum from the data produced by the sensor;

ii. perform a regression of the measured spectrum with a library of spectra;

iii. generate estimated mixing coefficients from the regression;

iv. compute a residual error between an estimated spectrum generated from the estimated mixing coefficients and the measured spectrum;

v. identify peaks in the residual error that extend in a direction opposite to that of peaks in the measured spectrum;

vi. perform a regression on the peaks to produce retro-regression coefficients;

vii. compute corrected mixing coefficients based on the retro-regression coefficients; and

viii. repeat (iv) through (vii) with the corrected mixing coefficients computed in (vii) being used to generate a new estimated spectrum for computing the residual error in (iv) at the next iteration.

18. The system of claim 17, wherein the processor is programmed to remove a member of the library whose mixing coefficient in the corrected mixing coefficients is less than a threshold.

19. The system of claim 18, wherein the processor is programmed to perform a regression of the measured spectrum with the library without the member that was removed to produce new mixing coefficients, and repeating (iv) through (vii) with the new mixing coefficients being used to generate a new estimated spectrum for computing the residual error at the next iteration.

20. The system of claim 17, wherein the processor is programmed to compute the corrected mixing coefficients by subtracting the retro-regression coefficients from the mixing coefficients for the estimated spectrum used in computing the residual error in the current iteration.

21. A method for processing spectroscopic measured data of a sample, comprising:

a. identifying peaks in a residual error between measured data and an estimated data computed from a regression performed on the measured data, wherein the peaks extend in a direction opposite to that of peaks in the measured data;

b. performing a regression on the peaks;

c. computing a corrected data based on the regression of the peaks;

d. computing a new residual error between the measured data and the corrected data; and

e. repeating (a) through (d) using the new residual error.

22. The method of claim 21, wherein (a) identifying comprises identifying a peak as at least a predetermined number of contiguous points that are on the opposite side, with respect to a baseline, to peaks in the measured signal.

23. The method of claim 22, wherein (e) repeating comprises repeating (a) through (d) until there are no more regions in the residual error having at least the predetermined number of contiguous points.

24. The method of claim 21, wherein (c) computing comprises subtracting the retro-regression coefficients from mixing coefficients for the estimated data.

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