Spectrochimica Acta Part A: Molecular and Biomolecular Spectroscopy 318 (2024) 124473

Contents lists available at ScienceDirect

Spectrochimica Acta Part A:
Molecular and Biomolecular Spectroscopy

journal homepage: www.journals.elsevier.com/spectrochimica-acta-part-a-molecular-and-biomolecular-spectroscopy

Baseline correction for the infrared spectra of exhaled breath

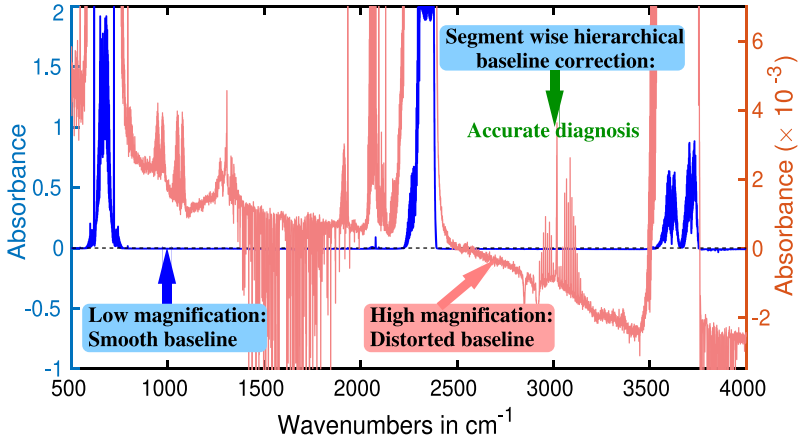
Susmita Roy [a], Kiran Sankar Maiti [b,c,*]

[a] Technical University of Munich, School of Medicine and Health, Department of Clinical Medicine, Klinikum rechts der Isar, Ismaninger Str. 22, 81675 Munich, Germany
[b] Department of Chemistry, Technical University of Munich, Lichtenbergstr. 4, D-85747 Garching, Germany
[c] Max–Planck-Institut für Quantenoptik, Hans-Kopfermann-Straße 1, 85748 Garching, Germany

HIGHLIGHTS

- VOCs in exhaled breath provide information about internal chemistry of the body.
- IR spectroscopy is a promising technique for the identification of VOCs in breath.
- Due to the presence of trace amount VOCs, in data processing, baseline looks distorted.
- Proposed hierarchical correction method allows accurately identify and quantify VOCs.

GRAPHICAL ABSTRACT



ARTICLE INFO

Keywords:
Infrared spectroscopy
Spectral baseline
Volatile organic compound (VOC)
Breath analysis
Component analysis
Spectral fingerprint
Biomarker

ABSTRACT

Infrared spectroscopy appears to be a promising analytical method for the metabolic analysis of breath. However, due to the presence of trace amounts in exhaled breath, the absorption strength of the metabolites remains extremely low. In such low detection limits, the nonlinear detection sensitivity of the infrared detector and electronic noise strongly modify the baseline of the acquired infrared spectra of breath. Fitting the reference molecular spectra with the baseline-modified spectral features of breath metabolites does not provide accurate identification. Therefore, baseline correction of the acquired infrared spectra of breath is the primary requirement for the success of breath-based infrared diagnosis. A selective spectral region-based, simple baseline correction method is proposed for the infrared spectroscopy of breath.

1. Introduction

Breath analysis is gradually gaining ground as a health monitoring and diagnostic tool for many diseases, particularly those that remain asymptomatic in the initial stages of the disease [1–3]. The unique advantage of breath-based diagnosis is its non-invasive sample collection [4–7]. Additionally, its rapid sample processing capability makes the method more advantageous than many traditional biofluid analysis techniques [8–10]. Above all, sample collection is extremely patient-friendly, making it a promising attractive screening method. In breath analysis, a composition of volatile metabolites (volatile or-

* Corresponding author at: Max–Planck-Institut für Quantenoptik, Hans-Kopfermann-Straße 1, 85748 Garching, Germany.
E-mail address: kiran.maiti@mpq.mpg.de (K.S. Maiti).

https://doi.org/10.1016/j.saa.2024.124473
Received 7 February 2024; Received in revised form 22 April 2024; Accepted 14 May 2024
Available online 21 May 2024

ganic compounds: VOCs) in exhaled breath is routinely analysed. The concentration of individual metabolites and their temporal evolution are both important for the development of breath-based screening and diagnostic methods [11,12].

Various techniques are rapidly developing to become reliable breath-based diagnostic methods. In this regard, gas chromatography–mass spectrometry (GC–MS) stands out as a pioneering analytical tool that already makes significant contributions to breath research [13]. However, due to the underdeveloped sample preparation procedure, GC–MS has not yet established itself as a diagnostic method for clinical applications [14]. Additionally, the high cost and bulky size of the GC–MS instrument, make it disadvantageous for clinical applications. The electronic nose (e-nose), which is developing to mimic the human olfactory system by using a set of chemical sensors, appears to be a much more promising screening method in regard to cost and device size [15]. However, it has not yet been able to produce consistent results across different research groups and is unable to identify the metabolites [16]. Another promising technology, the laser spectroscopy-based multi-wavelength UV photoacoustic is in its early developing stage and has shown success in application for respiratory diseases [17,18]. However, it is not clear yet, how to disentangle overlapping spectral features and identify corresponding metabolites. Therefore, a rigorous examination is necessary before accepting it as a diagnostic tool for clinical application. In these circumstances, infrared spectroscopy of breath is developing to overcome the above-mentioned shortfalls.

In fact, infrared spectroscopy holds all promises to be an appropriate analytical tool for breath research [19–22]. It utilizes the most fundamental molecular properties, e.g., molecular vibrations, as a probe to identify the molecule via structural analysis [23–25]. In experimental spectra, each vibrational band of a molecule is identified by unique spectral features. In the realm of clinical spectroscopy, these distinct spectral features are usually referred to as the ”fingerprints” of the molecule [26–28]. The precise characteristics, including the position, intensity, and morphology of the molecular fingerprints are the essential components for the development of infrared spectroscopy for breath [23,29]. However, two major challenges must be addressed to develop infrared spectroscopy-based breath diagnosis tools. Firstly, a large amount of water contained in an exhaled breath sample poses a significant obstacle to the application of infrared spectroscopy in breath [30,31]. Thanks to the recent development of water suppression technique from gaseous biofluids [32], there has been a substantial (factor of 2500) reduction of water vapour from the exhaled breath sample at −60 °C. The substantial reduction in water interference reveals numerous molecular patterns within breath samples, enabling the utilization of exhaled breath for disease diagnosis [19]. However, due to the extremely low concentrations of metabolites in exhaled breath, significant amplification along the absorption axis (y-axis) is essential to detect spectral characteristics. This amplification poses a challenge as it results in a non-flat spectral baseline, complicating the identification of metabolites when overlaying reference molecular spectra. Typically, these reference spectra, sourced from spectral databases or theoretically generated, which usually have smooth baselines [33–35]. Consequently, the least squares fitting method for distorted spectral features becomes inefficient and may lead to misinterpretations during metabolic identification. Therefore, a baseline correction is imperative for accurately interpreting observed spectral characteristics. In this paper, we propose a straightforward hierarchical baseline correction technique tailored for infrared spectroscopy of breath samples.

2. Nature of baseline for infrared spectra of breath

The infrared absorption spectra of the water-suppressed exhaled breath of a healthy adult are presented in Fig. 1 using two different magnifications on the absorption axes of the spectra. The blue colour line utilizes minimal magnification, with the corresponding absorption strength presented by the blue colour scale on the left side of the figure. The baseline for this plot appears perfectly flat, coinciding with the zero line. In three spectral regions (centred at 670, 2350, and 3600 cm^{-1}), strong absorption peaks are observed, all corresponding to different vibrational absorption bands of carbon dioxide (CO_2), which are less significant in the infrared diagnosis of breath [36]. Apparently, there is no further absorption peak in the blue colour spectra. The same spectra are further magnified by three orders of magnitude along the absorption axis and plotted using a red colour line in Fig. 1. The corresponding scale is positioned on the right side of the plot using the red colour. In the red colour spectrum, many spectral features of breath become apparent, which are not observed in the blue colour plot. However, in this plot, the baseline looks completely different from the blue colour plot. The baseline of the red colour plot is not only tilted but also distorted in various spectral regions. The distortion and tilt of the baseline significantly modify the individual spectral features, making the fitting of reference molecular spectra for the identification of metabolites considerably challenging. Therefore, for an accurate analysis of the breath metabolites, correcting the baseline of the infrared spectrum of breath is absolutely necessary.

3. Methods

In order to perform the baseline corrections, we propose a hierarchical correction procedure. The detail of the procedure is presented in the following three subsections.

3.1. First order baseline correction

The unprocessed infrared absorption spectrum of a breath sample is plotted in Fig. 2 using the dark grey colour line, labelled as “Original”. The baseline of the spectrum is shifted to the negative absorption (below zero line), which cannot be real. To perform the baseline correction, it is necessary to shift the baseline on or above the zero line, depending on the possible spectral behaviour. However, determining the amount of shifts poses a challenge. It is also observed that the baseline is tilted along the absorption axis. Therefore, a uniform linear shift is not sufficient for an efficient baseline correction. The best strategy is to find a spectral region, where no molecular absorption is observed and this spectral region should overlap with the zero line. Generally, none of the known molecules reveal absorption spectra in the spectral window between 2500–2800 cm^{-1}. Therefore, the plotted spectral data in this spectral window should perfectly overlap with the zero line. Practically, any data point in this spectral window can be chosen, the distance of the point from the zero line is measured, and finally, a similar amount of shift can be applied to the complete data set. However, due to electrical and electronic noise, a random fluctuation is observed throughout the spectrum. To avoid an over or under-shifting of the spectrum, a small spectral region is chosen between 2550 to 2600 cm^{-1}. A linear shift is calculated by averaging the y-values of all data points in this selected spectral window using the following equation,

$$LS = \frac{\sum y_i}{N} \qquad 2550 \le x_i \le 2600 \tag{1}$$

where, LS is the linear shift of the spectrum, x_i is the wavenumber value of the ith data point and the corresponding absorption value is y_i. N is the total number of data points in the selected spectral window. As a first step, the linear shift is applied to all data points in the entire spectral region. In our case, linear shift is applied in the spectral region between 500 to 4000 cm^{-1}. We refer to this linear baseline shift as the first-order baseline correction. The first-order baseline corrected spectrum is plotted using a blue colour line in Fig. 2.

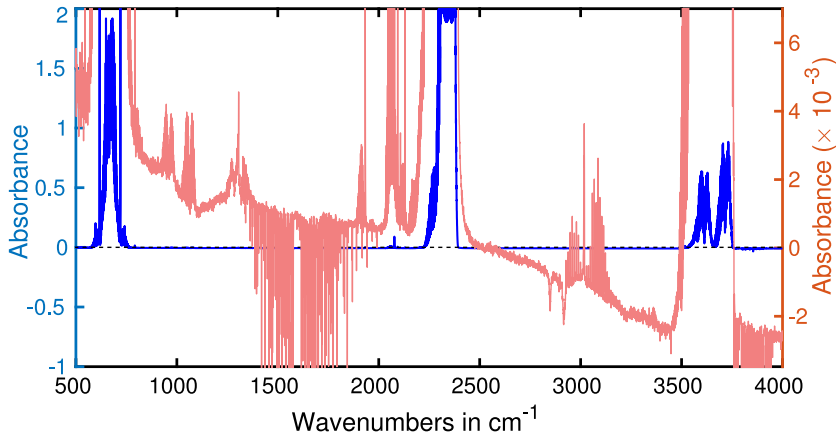


Fig. 1. The nature of spectral baseline of the infrared spectra of human exhaled breath. A minimal magnification is applied to the blue plot and the corresponding absorption strength is represented by the left-hand side scale of the plot. The same spectrum is plotted by magnifying three orders of magnitude using a red line. The corresponding absorption strength is scaled by the right-hand side scale. A linear shift is applied to the red line plot.

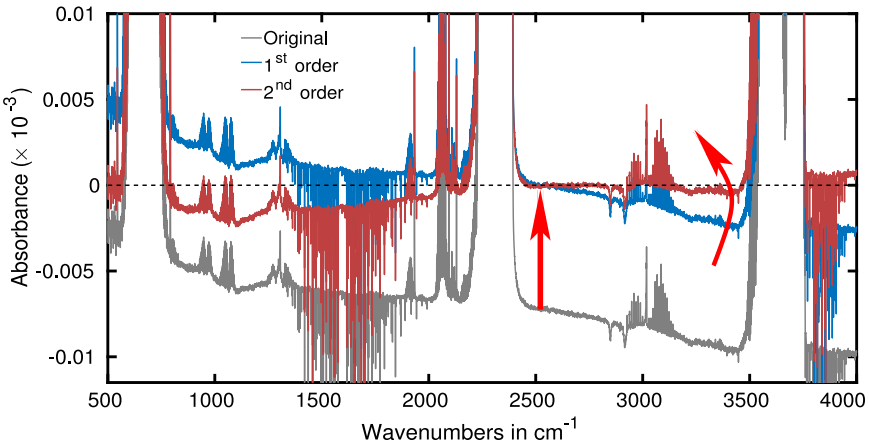


Fig. 2. Unprocessed infrared spectrum of exhaled breath is plotted by the dark grey line. The first-order correction of the breath spectrum is plotted using a light grey line. The reference point of linear shift is shown by the red arrow. The second-order baseline-corrected spectrum is plotted using the red colour line.

3.2. Second order baseline correction

Still, a general tilt of the spectrum need to be corrected for the acquired entire spectral span between 500–4000 cm^{-1}. The tilt of the spectrum can be corrected by rotating the spectrum across the zero line using the following equation.

$$AS_i = y_i - \frac{y_N - y_1}{N}(N - i) \qquad 500 \le x_i \le 4000 \tag{2}$$

Where AS_i is the angular shift of the ith point, N is the total number of data points, y_1 and y_N are the first and Nth (last) data values in the selected data set. After applying the angular shift, the spectrum is plotted using a red colour line. A significant part of the spectrum comes closer to the zero line with the application of this analytical method to the first-order corrected spectrum. Especially, the spectral window between 2500–2800 cm^{-1} coincides perfectly with the zero line. However, imperfections persist in many spectral regions. For instance, the spectral window between 900–2000 cm^{-1}, which is the most important spectral window, where many volatile metabolites in breath yield their characteristic infrared spectral features. The unique spectral feature of the molecule is commonly called the fingerprint of the molecule.

3.3. Third order baseline correction

Given that many spectral regions in the exhaled breath spectrum deviate from the zero line, further correction is necessary to rectify the baseline of the second-order baseline-corrected spectra. To enhance the spectral baseline further, we propose a segment-wise correction. A non-uniform deviation of the baseline is the primary reason for proposing a segment-wise correction method. Consequently, the selection of segments also exhibits non-uniformity. Determining the appropriate segment size is crucial for the success of the method and for the improved performance of breath-based diagnostics. Molecular vibrational spectroscopic knowledge is necessary for determining the appropriate segment sizes [37,38]. Molecular spectroscopists can efficiently determine the segment based on the breath-related individual molecular infrared spectra. Given the potential presence of hundreds of metabolites in breath, overlapping spectral features in the acquired breath spectra are highly probable. Theoretical and experimental individual molecular spectra assist in segment determination [9,39]. After identifying the segment, second-order corrections are applied to the spectral segment, assuming that, in a small spectral window, the baseline is linear. In the current state of breath-based diagnostic, close observation by molecular spectroscopists is necessary for accurate baseline correction. However, in the near future, the entire process

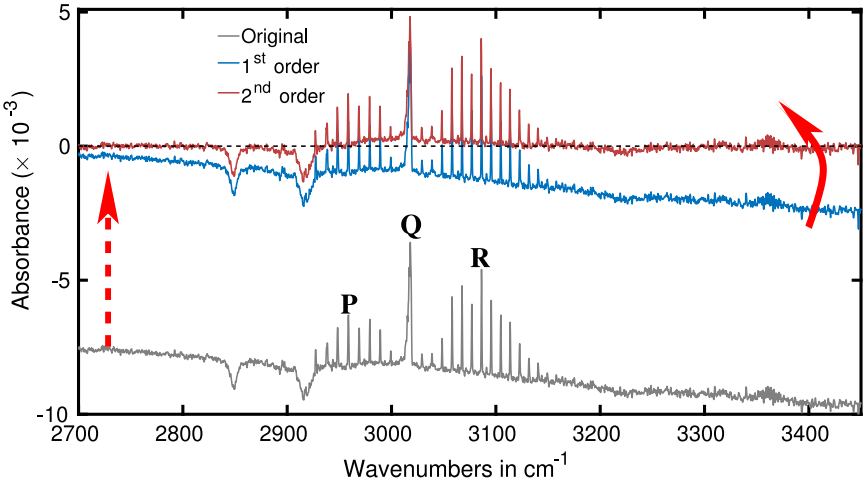


Fig. 3. Unprocessed infrared spectrum of breath around methane absorption band is plotted using a dark grey line. The corresponding first-order baseline corrected spectrum is plotted using a light grey line. The red colour plot represents the second-order baseline corrected spectrum.

can potentially be implemented using machine learning techniques, facilitating the development of automatic diagnostic methods [40,41].

It is important to note that the hierarchical baseline correction method outlined here comprises three sequential steps (Sections 3.1–3.3). Opting for a broader spectral window might render the first two correction steps are sufficient. However, in cases of narrower spectral windows, particularly within the molecular fingerprint region, employing all three steps becomes imperative.

4. Results and discussions

The described baseline correction methods are implemented in the breath spectra for the following molecular identifications.

4.1. Methane

Methane (CH_4) is a well-known greenhouse gas generally present in the atmosphere. During inhalation, each individual inhales methane from ambient air, and it is expected that they exhale a similar amount, unless it is absorbed by the body. However, methane concentrations tend to be notably higher in a subset of the adult population, confirming its endogenous origin [32,42]. This elevated methane concentration in exhaled breath is due to microbial fermentation in the human gastrointestinal tract [43]. Therefore, by analysing methane in human breath, it is possible to conclude on bacterial infection, provided that methane is accurately quantified.

The acquired methane spectra in breath are presented in Fig. 3 for a low methane emitter. The **P**, **Q**, and **R** branches of methane are clearly resolved even for low methane emitters. The unprocessed spectra (dark grey colour plot) exhibit a shift to negative intensity, which is unrealistic. In addition, the spectral baseline is tilted. Therefore, the least-square fitting cannot be readily applied to estimate the methane concentration. In these circumstances, baseline correction is essential to get a realistic methane concentration. After the first-order baseline correction spectra approach the zero line (blue colour spectrum); however, they still deviate with a slope of about 5° from the zero line. As a subsequent step, second-order correction is applied. The final baseline corrected spectrum is plotted using a red colour line. To demonstrate the goodness of the correction, the spectrum is plotted in a spectral window between 2700 and 3450 cm^{-1}, which is a rather broader spectral window. The baseline of the breath spectra appears well overlapped with the zero line. It seems third order baseline correction is not necessary for this spectral window. Up to second order correction of baseline allows fitting the reference methane spectrum to obtain the methane concentration in exhaled breath. The methane spectrum from the PNNL database serves as a reference spectrum. Using least-square fitting, the methane concentration is obtained approximately 450 ppb. This is rather low methane emission. In general, a large variation of methane concentration is observed in exhaled breath of individual, which typically vary from 400 ppb to 30 ppm[44,45].

4.2. Carbon monoxide

Carbon monoxide (CO) is one of the notable endogenous metabolites in human beings. Typically, CO is mainly generated by oxidative stress in the lung and inflammatory tissue injury [46]. It is considered as one of the biomarkers for several diseases like cancer, obesity, respiratory diseases, etc [47,48]. The concentration of CO in exhaled breath varies significantly due to the inhalation of atmospheric CO and smoking habits. Especially for moderate smokers, the exhaled breath CO concentration can be several times higher than that of non-smokers [12]. Therefore, error-free segregation of endogenous and external CO is crucial for precise disease diagnosis. In infrared spectra, the characteristic CO spectrum is observed around 2170 cm^{-1}. However, due to the overlap of water and CO infrared spectra, in general, it is not readily visible in the infrared spectra of human breath. In our experiment, effective water suppression enhances the visibility of the CO spectral feature. One example of water suppressed CO spectrum is presented in Fig. 4. The unprocessed CO spectrum is plotted with the blue colour line, and the corresponding absorption strength is scaled on the left side of the plot. The spectrum is not only shifted significantly below the zero line but also inclined up towards an increase in spectral wavenumber. The first-order correction is not shown here as it does not yield a substantial improvement. The second-order correction brings the baseline closer to zero line (grey colour plot), however, a slow rise of the baseline is still observed on the right side of the spectra. After applying the third-order correction, the spectral baseline overlaps very well with the zero line, represented by the red dashed line in the plot. It is important to note that both the second and third-order corrected spectra are scaled with the red scale on the right side of the plot.

4.3. Acetone

As an endogenous gaseous substance, acetone is considered an important metabolite for medical diagnosis. Generally, it is formed from fatty acid oxidation in cells and is released from the body through exhaled breath and other forms of biofluids like urine, sweat, etc. and produce a body odour. While acetone in exhaled breath typically shows a low concentration for healthy individuals, however, fasting significantly increases its concentration [12,49]. The distinct sweet

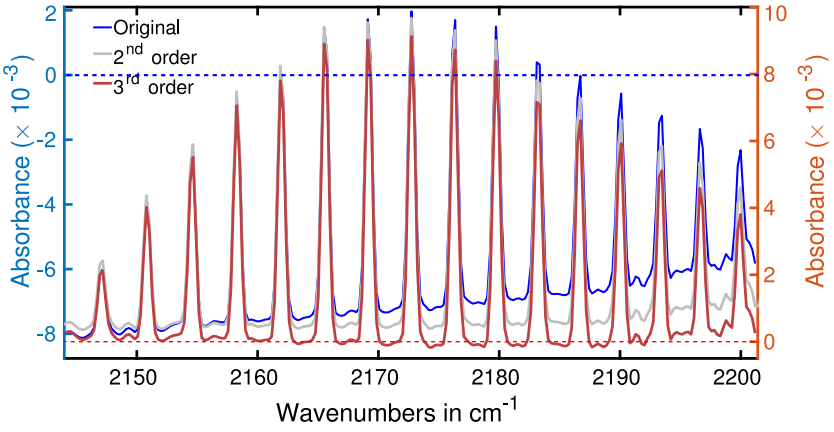


Fig. 4. Unprocessed infrared spectrum of carbon monoxide in breath is plotted using a blue colour line. The corresponding absorption scale is on the left-hand side. The scale and the zero line both are in blue. The first-order corrected plot is omitted from the figure. The second and third-order corrected spectra are plotted using light grey and red colour lines respectively. The scale for both plots is on the right side.

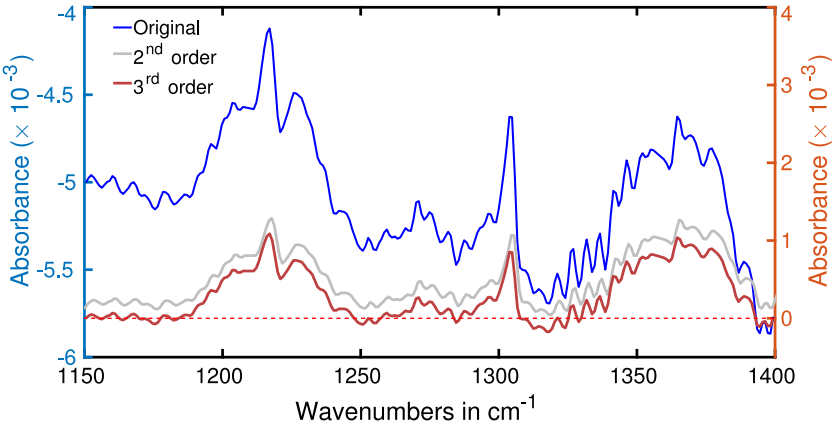


Fig. 5. Unprocessed infrared spectrum of breath in the spectral range between 1150 and 1400 cm^{-1} is plotted with a blue line. The corresponding absorption scale is on the left-hand side. The first-order corrected plot is omitted from the figure. The second and third-order corrected spectra are plotted using light grey and red lines respectively. The scale for both plots is on the right side.

odour associated with individuals with diabetes is well known to be attributed to a substantial rise in acetone level [50]. Although a large dynamic range of acetone concentration is reported by many researchers, for healthy individuals with regular lifestyles and diets, acetone concentration in exhaled breath remains below 1 ppb [51]. In infrared spectra, acetone is identified by two distinct peaks centred at 1217 cm^{-1} and 1365 cm^{-1}. The absorption spectra of breath in the above-mentioned spectral region are presented in Fig. 5. The spectral region is highly populated by many other molecular features. As a result, acetone spectral features are strongly modified. For example, the strong absorption peak is observed at 1300 cm^{-1}, which is identified as the **Q** of methane. The **R** branch of methane, situated on the right side of **Q** branch, significantly modifies the left side slop of the acetone peak at 1365 cm^{-1}. Additionally, many aldehyde molecules also modify this peak [9]. Water (remaining after water suppression) spectra and detection noise also influence this spectral region, resulting in a distorted baseline [52,53]. The unprocessed breath spectrum is plotted using a blue colour line in Fig. 5. The spectrum is significantly shifted to the negative absorption (as seen on the left side blue scale), and in addition, a tilt of the spectrum is observed. With the application of second-order correction, the baseline of the spectrum moves very close to the zero line. After applying third-order correction, the baseline matches very well with the zero line. The absorption scale of the corrected spectra is shown on the right of the plot.

5. Conclusions

The article proposes a straightforward baseline correction method for infrared spectra, focusing specifically on identifying breath metabolites. The low absorption strength of breath metabolites, attributed to their trace presence, is further complicated by the nonlinear detection sensitivity and electronic noise of the infrared detector. These factors distort the baseline of acquired infrared breath spectra, rendering the fitting of molecular spectra ineffective and making baseline correction a necessary step for the development of infrared spectroscopy-based diagnostics. While a few technical steps are involved, the primary strategy is to perform the correction segment-wise.

Despite the observed abrupt distortion in infrared spectra of breath, a small segment of the spectral region often retains a linear baseline. This approximation simplifies the correction procedure and has been successfully applied to extract metabolic information from infrared spectra of exhaled human breath. The article demonstrates the effectiveness of this correction method by applying it to representative spectral regions. During the developing stage of infrared spectroscopy-based breath analysis, close observation by molecular spectroscopists is necessary. However, this simple baseline correction method can be easily integrated into machine learning techniques for the automate data analysis

CRediT authorship contribution statement

Susmita Roy: Writing – review & editing, Writing – original draft, Visualization, Validation, Investigation, Formal analysis. **Kiran Sankar Maiti:** Writing – review & editing, Writing – original draft, Supervision, Formal analysis, Conceptualization.

Declaration of competing interest

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests: Kiran Sankar Maiti reports a relationship with LMU Munich that includes: employment. If there are other authors, they declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Data availability

Data will be made available on request.

Acknowledgements

There is no financial support involved with this article.

References

[1] S. Das, M. Pal, Review-non-invasive monitoring of human health by exhaled breath analysis: A comprehensive review, J. Electrochem. Soc. 167 (3) (2020) 037562, http://dx.doi.org/10.1149/1945-7111/ab67a6.

[2] K.S. Maiti, E. Fill, F. Strittmatter, Y. Volz, R. Sroka, A. Apolonski, Towards reliable diagnostics of prostate cancer via breath, Sci. Rep. 11 (2021) 18381, http://dx.doi.org/10.1038/s41598-021-96845-z.

[3] A. Sharma, R. Kumar, P. Varadwaj, Smelling the disease: Diagnostic potential of breath analysis, Mol. Diagn. Therapy 27 (3) (2023) 321–347, http://dx.doi.org/10.1007/s40291-023-00640-7.

[4] W. Cao, Y. Duan, Breath analysis: Potential for clinical diagnosis and exposure assessment, Clin. Chem. 52 (5) (2006) 800–811, http://dx.doi.org/10.1373/clinchem.2005.063545.

[5] K.S. Maiti, S. Roy, R. Lampe, A. Apolonski, Breath indeed carries significant information about a disease: Potential biomarkers of cerebral palsy, J. Biophotonics 13 (11) (2020) e202000125, http://dx.doi.org/10.1002/jbio.202000125.

[6] K.S. Maiti, A. Apolonski, Monitoring the reaction of the body state to antibiotic treatment against helicobacter pylori via infrared spectroscopy: A case study, Molecules 26 (11) (2021) http://dx.doi.org/10.3390/molecules26113474.

[7] A. Manolis, The diagnostic potential of breath analysis, Clin. Chem. 29 (1) (1983) 5–15, URL http://clinchem.aaccjnls.org/content/29/1/5.

[8] N.J. Rattray, Z. Hamrang, D.K. Trivedi, R. Goodacre, S.J. Fowler, Taking your breath away: Metabolomics breathes life in to personalized medicine, Trends Biotechnol. 32 (10) (2014) 538–548, http://dx.doi.org/10.1016/j.tibtech.2014.08.003.

[9] A. Apolonski, K.S. Maiti, Towards a standard operating procedure for revealing hidden volatile organic compounds in breath: The Fourier-transform IR spectroscopy case, Appl. Opt. 60 (14) (2021) 4217–4224, http://dx.doi.org/10.1364/AO.421994.

[10] J. Lim, A. Rezaie, Pros and cons of breath testing for small intestinal bacterial overgrowth and intestinal methanogen overgrowth, Gastroenterol Hepatol (N Y) 19 (3) (2023) 140–146.

[11] M. Phillips, J. Herrera, S. Krishnan, M. Zain, et al., Variation in volatile organic compounds in the breath of normal humans, J. Chromatogr. B: Biomed. Sci. Appl. 729 (1–2) (1999) 75–88, http://dx.doi.org/10.1016/S0378-4347(99)00127-9.

[12] K.S. Maiti, M. Lewton, E. Fill, A. Apolonski, Human beings as islands of stability: Monitoring body states using breath profiles, Sci. Rep. 9 (2019) 16167, http://dx.doi.org/10.1038/s41598-019-51417-0.

[13] B. Hu, Mass spectrometric analysis of exhaled breath: Recent advances and future perspectives, TRAC Trends Anal. Chem. 168 (2023) 117320, http://dx.doi.org/10.1016/j.trac.2023.117320.

[14] A.M. Ellis, C.A. Mayhew, Proton Transfer Reaction Mass Spectrometry: Principles and Applications, Wiley, 2013, http://dx.doi.org/10.1002/9781118682883.

[15] O.S. Kwon, H.S. Song, S.J. Park, S.H. Lee, et al., An ultrasensitive, selective, multiplexed superbioelectronic nose that mimics the human sense of smell, Nano Lett. 15 (10) (2015) 6559–6567, http://dx.doi.org/10.1021/acs.nanolett.5b02286.

[16] T. Liu, L. Guo, M. Wang, C. Su, et al., Review on algorithm design in electronic noses: Challenges, status, and trends, Intell. Comput. 2 (2023) http://dx.doi.org/10.34133/icomputing.0012.

[17] B. Henderson, A. Khodabakhsh, M. Metsälä, I. Ventrillard, et al., Laser spectroscopy for breath analysis: Towards clinical implementation, Appl. Phys. B 124 (8) (2018) http://dx.doi.org/10.1007/s00340-018-7030-x.

[18] V.R. Nidheesh, A.K. Mohapatra, V.B. Kartha, S. Chidangil, Multiwavelength photoacoustic breath analysis sensor for the diagnosis of lung diseases: COPD and asthma, ACS Sens. 8 (11) (2023) 4111–4120, http://dx.doi.org/10.1021/acssensors.3c01316.

[19] K.S. Maiti, Non-invasive disease specific biomarker detection using infrared spectroscopy: A review, Molecules 28 (5) (2023) http://dx.doi.org/10.3390/molecules28052320.

[20] B. Tuzson, H. Looser, F. Felder, F. Bovey, L. Tappy, L. Emmenegger, Human breath acetone analysis by Mid-IR laser spectroscopy: Development and application, in: High-Brightness Sources and Light-Driven Interactions, Optical Society of America, 2018, p. MT3C.3, http://dx.doi.org/10.1364/MICS.2018.MT3C.3.

[21] R. Selvaraj, N.J. Vasa, S.M.S. Nagendra, B. Mizaikoff, Advances in mid-infrared spectroscopy-based sensing techniques for exhaled breath diagnostics, Molecules 25 (9) (2020) 2227, http://dx.doi.org/10.3390/molecules25092227.

[22] F. Naz, A.G. Groom, M. Mohiuddin, A. Sengupta, et al., Using infrared spectroscopy to analyze breath of patients diagnosed with breast cancer, J. Clin. Oncol. 40 (16_suppl) (2022) e13579, http://dx.doi.org/10.1200/JCO.2022.40.16_suppl.e13579.

[23] K.S. Maiti, Vibrational spectroscopy of Methyl benzoate, Phys. Chem. Chem. Phys. 17 (2015) 19735–19744, http://dx.doi.org/10.1039/C5CP02281A.

[24] E. Wilson, J. Decius, P. Cross, Molecular Vibrations: The Theory of Infrared and Raman Vibrational Spectra, Dover Books on Chemistry Series, Dover Publications, New York, 1980, URL https://books.google.de/books?id=CPkvsDrPiv0C.

[25] A. Szabo, N.S. OstlundBaker, Modern Quantum Chemistry : Introduction to Advanced Electronic Structure Theory, Dover publications, Mineola (N.Y.), 1996, URL https://lib.ugent.be/catalog/rug01:000906565.

[26] J. Yang, Y. Cai, K. Zhao, et al., Concepts and applications of chemical fingerprint for hit and lead screening, Drug Discov. Today 27 (11) (2022) 103356, http://dx.doi.org/10.1016/j.drudis.2022.103356.

[27] K.S. Maiti, Analysis of volatile metabolites using vibrational spectroscopy, Eng. Proceed. 51 (1) (2023) 46, http://dx.doi.org/10.3390/engproc2023051046.

[28] J.H. Shorter, D.D. Nelson, J.B. McManus, M.S. Zahniser, D.K. Milton, Multicomponent breath analysis with infrared absorption using room-temperature quantum cascade lasers, IEEE Sens. J. 10 (1) (2010) 76–84.

[29] C. Mansfield, H. Mantsch, H. Rutt, Application of infrared spectroscopy in the measurement of breath trace compounds: A review, Can. J. Anal. Sci. Spectr. 47 (1) (2002) 14–28, URL https://eprints.soton.ac.uk/21007/.

[30] J. Zieliński, J. Przybylski, How much water is lost during breathing? Pneumonol Alergol. Pol. 80 (4) (2012) 339–342.

[31] K.S. Maiti, E. Fill, F. Strittmatter, Y. Volz, R. Sroka, A. Apolonski, Standard operating procedure to reveal prostate cancer specific volatile organic molecules by infrared spectroscopy, Spectrochimica Acta Part A: Mol. Biomol. Spectrosc. 304 (2024) 123266, http://dx.doi.org/10.1016/j.saa.2023.123266.

[32] K.S. Maiti, M. Lewton, E. Fill, A. Apolonski, Sensitive spectroscopic breath analysis by water condensation, J. Breath Res. 12 (4) (2018) 046003, http://dx.doi.org/10.1088/1752-7163/aad207.

[33] T.J. Johnson, R.L. Sams, S.W. Sharpe, The PNNL quantitative infrared database for gas-phase sensing: A spectral library for environmental, hazmat, and public safety standoff detection, in: A.J. Sedlacek, R. Colton, T. Vo-Dinh (Eds.), in: Chemical and Biological Point Sensors for Homeland Defense, vol. 5269, 2004, pp. 159–167, http://dx.doi.org/10.1117/12.515604.

[34] I. Gordon, L. Rothman, C. Hill, R. Kochanov, et al., The HITRAN2016 molecular spectroscopic database, J. Quant. Spectrosc. Radiat. Transfer 203 (2017) 3–69, http://dx.doi.org/10.1016/j.jqsrt.2017.06.038, HITRAN2016 Special Issue.

[35] A. Kramida, Y. Ralchenko, J. Reader, NIST ASD Team, NIST Atomic Spectra Database (ver. 5.7.1), National Institute of Standards and Technology, Gaithersburg, MD, 2019, [Online]. Available: https://physics.nist.gov/asd. (9 April 2017).

[36] A. Apolonski, S. Roy, R. Lampe, K.S. Maiti, Molecular identification of bio-fluids in gas phase using infrared spectroscopy, Appl. Opt. 59 (17) (2020) E36–E41, http://dx.doi.org/10.1364/AO.388362.

[37] K.S. Maiti, C. Scheurer, Basis set extrapolation for the high resolution spectroscopy, J. Chem. Chem. Eng. 7 (2013) 1100–1110, http://dx.doi.org/10.17265/1934-7375/2013.11.014.

[38] S. Roy, K.S. Maiti, Structural sensitivity of CH vibrational band in methyl benzoate, Spectrochim. Acta Mol. Biomol. Spectrosc. 196 (2018) 289–294, http://dx.doi.org/10.1016/j.saa.2018.02.031.

[39] M.F. Gelin, A.P. Blokhin, E. Ostrozhenkova, A. Apolonski, K.S. Maiti, Theory helps experiment to reveal VOCs in human breath, Spectrochimica Acta Part A: Mol. Biomol. Spectrosc. (2021) 119785, http://dx.doi.org/10.1016/j.saa.2021.119785.

[40] P. Ghosh, B. Chaudhury, S. Purohit, V. Joshi, A. Kothari, D. Shetranjiwala, Deep learning assisted microwave-plasma interaction based technique for plasma density estimation, J. Phys. D: Appl. Phys. 57 (1) (2023) 014001, http://dx.doi.org/10.1088/1361-6463/acfdb6.

[41] M. Schinkel, A.W. Boerman, K. Paranjape, W.J. Wiersinga, P.W. Nanayakkara, Detecting changes in the performance of a clinical machine learning tool over time, eBioMedicine 97 (2023) 104823, http://dx.doi.org/10.1016/j.ebiom.2023.104823.

[42] C. Kumpitsch, F.P.S. Fischmeister, A. Mahnert, et al., Reduced B12 uptake and increased gastrointestinal formate are associated with archaeome-mediated breath methane emission in humans, Microbiome 9 (1) (2021) http://dx.doi.org/10.1186/s40168-021-01130-w.

[43] G.A. Weaver, J.A. Krause, T.L. Miller, M.J. Wolin, Incidence of methanogenic bacteria in a sigmoidoscopy population: An association of methanogenic bacteria and diverticulosis, Gut 27 (6) (1986) 698–704, http://dx.doi.org/10.1136/gut.27.6.698.

[44] K. Dryahina, D. Smith, P. Španěl, Quantification of methane in humid air and exhaled breath using selected ion flow tube mass spectrometry, Rapid Commun. Mass Spectrom. 24 (9) (2010) 1296–1304, http://dx.doi.org/10.1002/rcm.4513.

[45] D. Polag, F. Keppler, Long-term monitoring of breath methane, Sci. Total Environ. 624 (2018) 69–77, http://dx.doi.org/10.1016/j.scitotenv.2017.12.097.

[46] S.W. Ryter, J.M. Sethi, Exhaled carbon monoxide as a biomarker of inflammatory lung disease, J. Breath Res. 1 (2) (2007) 026004, http://dx.doi.org/10.1088/1752-7155/1/2/026004.

[47] S.W. Ryter, A.M.K. Choi, Carbon monoxide: Present and future indications for a medical gas, Korean J. Intern. Med. 28 (2) (2013) 123–140, http://dx.doi.org/10.3904/kjim.2013.28.2.123.

[48] P. Paredi, W. Biernacki, G. Invernizzi, S.A. Kharitonov, P.J. Barnes, Exhaled carbon monoxide levels elevated in diabetes and correlated with glucose concentration in blood: A new test for monitoring the disease? Chest 116 (4) (1999) 1007–1011, http://dx.doi.org/10.1378/chest.116.4.1007.

[49] A. Jones, Breath-Acetone Concentrations in Fasting Healthy Men: Response of Infrared Breath-Alcohol Analyzers, J. Anal. Toxicol. 11 (2) (1987) 67–69, http://dx.doi.org/10.1093/jat/11.2.67.

[50] Z. Wang, C. Wang, Is breath acetone a biomarker of diabetes? A historical review on breath acetone measurements, J. Breath Res. 7 (3) (2013) 037109, http://dx.doi.org/10.1088/1752-7155/7/3/037109.

[51] C. Turner, P. Španěl, D. Smith, A longitudinal study of breath isoprene in healthy volunteers using selected ion flow tube mass spectrometry (SIFT-MS), Physiol. Meas. 27 (1) (2006) 13, http://dx.doi.org/10.1088/0967-3334/27/1/002.

[52] A.P. Fellows, M.T. Casford, P.B. Davies, Spectral analysis and deconvolution of the amide I band of proteins presenting with high-frequency noise and baseline shifts, Appl. Spectrosc. 74 (5) (2020) 597–615, http://dx.doi.org/10.1177/0003702819898536.

[53] F. Zhang, X. Tang, L. Li, Origins of baseline drift and distortion in Fourier transform spectra, Molecules 27 (13) (2022) 4287, http://dx.doi.org/10.3390/molecules27134287.