# Analysis of Exhaled Human Breath via Terahertz Molecular Spectroscopy

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***Abstract*—We report on our progress in utilizing THz breath sensing in several bio-medical diagnostic applications. Our work bears promise in applying this technology to non-invasive analysis of blood glucose based on chemical composition of breath, as well as assessment of asthma related airway inflammation. Our most recent testing of CMOS based THz breath sensor, in the evolution of this technology towards compact and affordable implementations, is discussed.**

## I. INTRODUCTION

Chemical sensors utilizing high resolution THz rotational spectra offer significant benefits for molecular identification in terms of sensitivity and facilitate near 'absolute' specificity of detecting many species. THz breath sensor at Wright State University (WSU) (Figure 1) utilizes solid state multiplier transmitter (TX) and heterodyne receiver (RX) made by Virginia Diodes, Inc. (VDI), as well as commercial and custom built preconcentration devices to extract valuable analytes from exhaled human breath [3]. Our laboratory system can currently detect and quantify acetone, ethanol, methanol, acetaldehyde, hydrogen cyanide, chloromethane, isoprene, dimethyl sulfide, and formaldehyde via analysis of 1L of human breath (few exhalations), with many more breath chemicals suitable for THz detection.

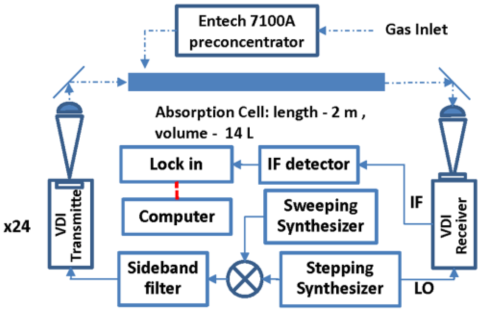

**Fig. 1.** Block Diagram of the system [1, 2].

## II. RESULTS

Over the course of past two years our research team worked on advancing the technology and science to gain a foothold in a promising bio-medical application domain. To demonstrate analytical capabilities of THz chemical sensors, we conducted a comparative analysis of breath samples using THz sensor and state of the art Gas Chromatography - Mass Spectrometry commercial facility (ALS Environmental). Figure 2 shows good correspondence of THz and GC-MS measurements for acetone. Multiple THz measurements for each sample were conducted, showing good reproducibility of THz sampling. For several breath species (Acetaldehyde and Ethanol) THz sampling showed consistently higher dilutions, which speaks

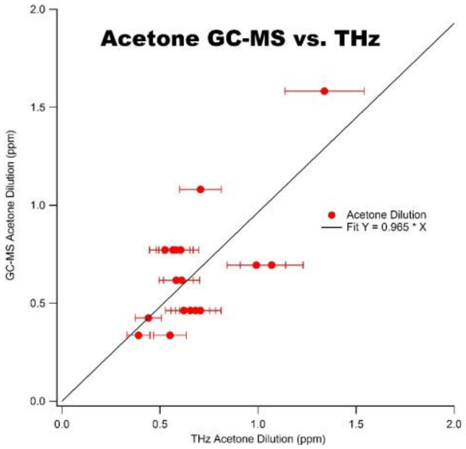

**Fig. 2** Comparison between measurement of breath acetone dilution using WSU THz breath sensor (horizontal scale) and a commercial GC-MS facility (ALS Environmental).

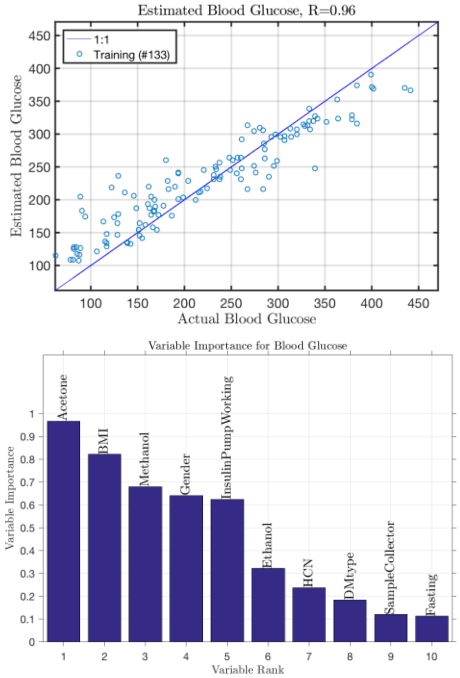

**Fig. 3.** Estimation of Blood Glucose using a non-parametric machine learning algorithm capable of predicting blood sugar level based on THz breath chemical dilutions and several bio-metric parameters (top). Ranking of parameter space in order of their importance to the learning algorithm (bottom)

for lower recovery in the GC-MS measurements.

In our recent project funded by Samsung we focused on applying THz breath sensing to non-invasively gauge blood glucose levels in Type I diabetic patients. We have acquired and analyzed nearly 150 breath samples from volunteers at WSU and patients at UT Southwestern Medical Center. Development of robust predictive algorithms of blood glucose based on breath sensing is a challenging project. Breath acetone strongly correlates with blood glucose in Type I diabetic, but by itself acetone concentration is not an exclusive predictor of blood sugar level. In our research we determined that predictive algorithms need to go beyond traditional least squares fitting, so we invoked a non-parametric machine learning methods to understand the feasibility of using these techniques for non-invasive glucose assessment. Figure 3 shows encouraging results of this effort and demonstrate the prediction of blood glucose with an R-value of 0.96. This result needs to be taken cautiously, since machine learning algorithms are most suitable for reductions of significantly larger datasets (>>150). Nonetheless, our method resulted in an adequately accurate predictive scheme with 10 input parameters shown in the bottom section of Figure 3. We discovered that breath acetone, methanol, and body-mass-index are the main, so far accounted for, predictors of blood glucose. But apparent complexity of blood glucose metabolism calls for further development of predictive algorithms and expansion of the parameter base.

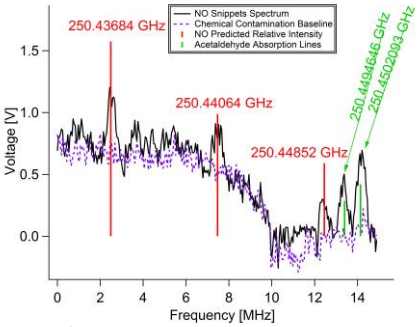

**Fig. 4** THz detection of breath NO. Black trace: breath spectrum. Purple trace: chemical background of the system. Red and green lines: Catalogued positions of NO and acetaldehyde respectively.

Our preliminary results hold promise in utilizing this technology to detect chemicals related to air-way inflammation of which NO is known as a predictor of asthma. Figure 4 shows our most recent detection of NO in human breath at part-per-billion level of dilution.

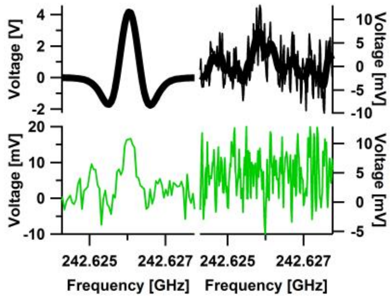

**Fig. 5.** Detection of ethanol at 44 ppm from 1 L of breath with VDI based TX/RX (S/N ~ 1000, left) and CMOS based TX/RX (S/N ~ 3, right). Black trace - spectrum with breath samples, Green trace - spectrum of evacuated cell. Integration time per point is 0.1s for VDI and 8s for CMOS based system. Estimated ethanol pressure ~ 2mtorr.

Most recently we demonstrated fist ever chemical analysis of human breath using a fully integrated CMOS based TX/RX modules developed by University of Texas at Dallas (UTD) [4] (right side of Figure 5). Figure 6 shows that noise characteristics of the CMOS TX/RX circuits are well suited for high resolution spectral acquisition. Left side of Figure 6 demonstrates detection of methyl mercaptan with a full power to noise ratio of 6000/Hz$^{1/2}$, while right side corresponds to 1200/Hz$^{1/2}$ detection. Side by side comparison with the VDI based system (left side of Figure 5) helped us identify modification of the CMOS based TX/RX that will allow it to bridge the apparent (~3000) gap in sensitivity: 1. Better coupling of the power from the CMOS RX module to free space and to the TX module, 2. Refinement of the onboard amplification to warrant best noise characteristics of the CMOS circuitry.

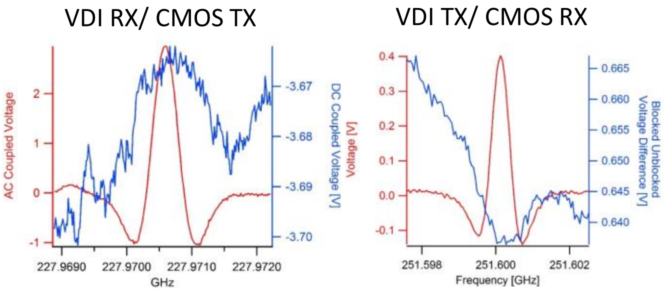

**Fig. 6.** Detection of methyl mercaptan using CMOS TX/VDI RX (left) and VDI TX/CMOS RX (right), both demonstrating excellent phase noise characteristics of the CMOS circuitry.

## III. SUMMARY

We made significant progress in assessing the capabilities of THz breath sensing and development of CMOS based THz devices, which positions us to develop an affordable table-top THz breath sensor in the near future. Our vision of the application domain spans medical, military, and civilian sectors. Comparison with Mass-Spectrometry based gas analyzers, that dominate gas sensing market, is very favorable and make us optimistic about the imminent adoption of this technology by analytical gas sensing community. We thank Samsung and Air Force Office of Scientific Research for ongoing support.

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