Dual-modulation Faraday Rotation Spectrometer for Real-time Detection of Nitric Oxide (NO) Isotopes in Human Breath, and Nitrate/Nitrite in Urine/Blood

E. Zhang, Y. Wang, M. Nikodem, G. Wysocki*
Electrical Engineering Department, Princeton University, Princeton, NJ 08540, USA
*gwysocki@princeton.edu

A new Faraday rotation spectroscopy (FRS) sensor system that allows performing measurements of nitric oxide (NO) isotopes with sensitivities approaching the fundamental quantum limits is presented. A novel dual modulation FRS signal detection technology (DM-FRS, U.S. Patent No. 8,947,663) enables implementation with a relatively simple opto-mechanical configuration that allows construction of robust and reliable instruments suitable for wide variety of measurement conditions (e.g. in clinical settings). Preliminary tests of the first generation DM-FRS prototype have been completed at Cleveland Clinic, where NO isotopic detection in breath, urine, and blood were utilized for metabolic studies, demonstrating promise for future applications in noninvasive medical diagnostics.

Nitric oxide (NO) is a highly reactive radical species that plays an important role in many chemical processes ranging from atmospheric chemistry (e.g. ground ozone formation) to bio-medical science. Due to its high reactivity NO occurs at very low concentrations and its detection at sub-ppbv levels is often desired. Here we present a spectroscopic sensor system, which employs a quantum cascade laser source operating at 5.4 μm (from Alpes Laser SA), and uses a novel DM-FRS technique for signal-to-noise enhancement, yielding ^{14}NO and ^{15}NO detection limits of 3.84 and 0.53 ppbv/Hz$^{1/2}$, respectively.

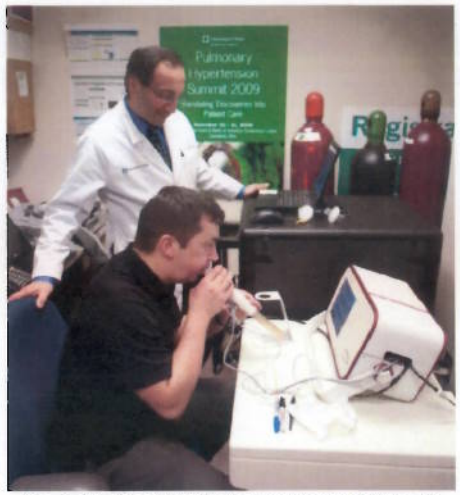

Fig. 1: Dr. Raed Dweik (top) and Gerard Wysocki testing the instrument at Cleveland Clinic, Cleveland, OH, 2013 (Photo by Yin Wang)

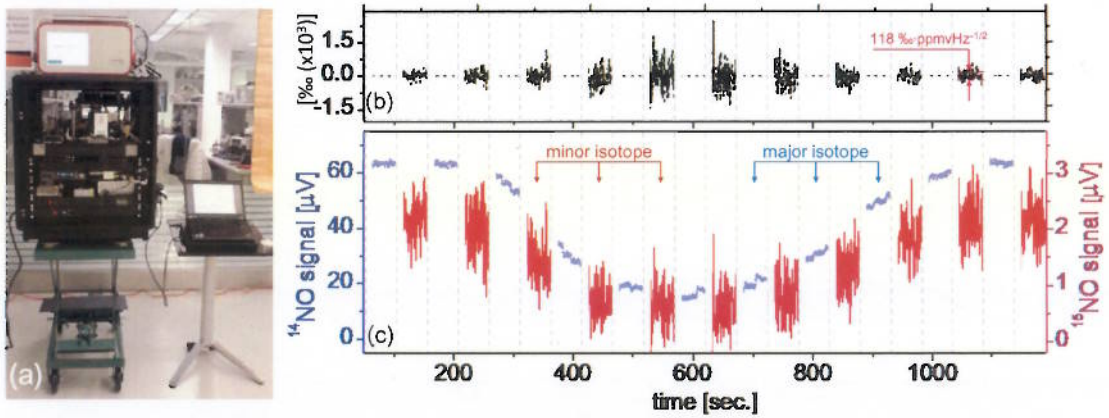

Fig. 2: (a) Second generation transportable prototype. (b) Ratiometric analysis by linear interpolation of ^{14}NO during ^{15}NO measurement times. For 1 ppmv ^{14}NO sample, 118‰·ppmv·Hz$^{-1/2}$ deviations are calculated. (c) Time-multiplexed measurements of ^{14}NO, ^{15}NO using 50 s intervals (40% duty cycle).

Signal processing and control is performed using a single digital lock-in amplifier unit (Zurich Instruments HF2LI). The instrument is interfaced with a Loccioni® breath analyzer for detection of NO isotopes monitored together with CO_2, and airway pressure. System enhancements have resulted in a current second-generation prototype housed within a transportable 19" rack-mounted system (fig. 2(a)), with significant potential for further miniaturization. Quasi-simultaneous isotope measurements are demonstrated via line-switching between ^{14}NO and ^{15}NO at 50 sec. intervals and a duty cycle of 40% per isotope (Fig. 2(c)), using a controlled dilution of approximately 1 ppm ^{14}NO gas.

Linear interpolation of the ^{14}NO concentrations during ^{15}NO measurements enable ratiometric analysis (Fig. 2(b)), yielding a ratiometric precision of approximately 118 ‰·ppmv·Hz$^{-1/2}$, normalized to sample concentration. Our custom nitrate/nitrite to NO conversion system provides ^{14}NO concentrations above 10 ppmv, which combined with > 100 s averaging will provide ~1.2 ‰ ratiometric precision.

Acknowledgements: We would like to thank Dr. Raed Dweik at Cleveland Clinic, Dr. Christina Kao at Baylor College of Medicine and Prof. Daniel Sigman for fruitful discussions and collaboration on instrument testing.