Volume 18, Number 1 ◆ Spring 2002

Research Report

Precision Low-Coherence Interferometry For Cell Biology Applications

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Introduction The low-coherence interferometry program at the Spectroscopy Laboratory has developed several novel techniques for studying the structure, organization and dynamics of biological cells. These techniques exploit the low-coherence properties of broadband light to permit depth resolved imaging. Our new techniques represent advances in low-coherence interferometry, as they provide a means for examining not only the amplitude of a scattered light field but also its wave properties, such as coherence and phase. By obtaining information about these wave properties, our new techniques are proving to be powerful tools for laboratory cell biology studies.

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Angle-Resolved Low Coherence Interferometry Angle-resolved low coherence interferometry (a/LCI), our novel technique for measuring the angular distribution of backscattered light, provides a means for studying both the structure and organization of biological cells. The a/LCI technique can be viewed as an interferometric implementation of light scattering spectroscopy (LSS), a method for deducing cellular structure based on examining the wavelength dependence of scattered light. Both a/LCI and LSS examine the momentum transferred in the elastic scattering process. However, while LSS uses a spectrograph or filters to resolve the scattered light by wavelength, a/LCI exploits spatial coherence to resolve the scattered light by angle. Further, while LSS uses modeling or polarization gating to reject multiply scattered light, which acts as a source of noise in these types of measurements, a/LCI exploits the temporal coherence of the broadband source to isolate the light scattered by localized structures, even beneath the surface of tissues.

The a/LCI scheme (Figure 1) is based on a modified Michelson interferometer [1]. Broadband light from a superluminescent diode is divided by a beamsplitter (BS) into a reference beam and an input beam to the sample. The reference beam is reflected by a mirror (M) and recombined at BS with light scattered by the sample. The mixed fields generate an interference pattern provided that the two optical path lengths are matched to within the coherence length of the source.

The a/LCI spectra depict the interference signal as a function of scattering angle, referenced to the exact backscattering direction. The a/LCI system employs four achromatic imaging lenses

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Comment

Dealing With Terrorism: Technology Can Help, But It Is Not Enough

Martin Hunter
GR Harrison Spectroscopy Laboratory, MIT

"*He who knows, but doesn't act, doesn't know*." - Chinese proverb

Four months have already passed since the terrible events of September 11, and I find myself increasingly caught up again in my regular, daily routines. My conscience chides me for it, and prods for an answer to the question: What am I doing differently? What lasting changes have been imparted or decided upon, following that experience of intense sadness, shock and anxiety?

The sheer weight of such a ponderous question would normally make me keel over, defeatedly admitting "Not enough!" In honesty, my answer still is "Not enough!", but there is a definite change of tone this time around. I am surprised at the clarity with which I see changes in my perspective which have occurred since September 11, and the resolve with which I intend to follow and uphold them: an increased awareness of the joy and sanctity of life; a focused commitment to pursuing my ideals of peace and justice; and a budding sense of the essential need for community.

I cannot escape the fact that there are people in the world who opt for violent means of expression or fulfilment of their aims. In response to this, I think it is natural to implement preventive measures for identifying and protecting against any such

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Personalities

Adam Wax

An Interview by Judi Sheytanian

Adam Wax was born in New York City and grew up in Great Neck, a small town on Long Island. During his early years in public school, Adam found he was not very challenged as a student. As a result, he found ways to stimulate his interests by experimenting around the house. Although his curious nature was often construed as troublemaking, Adam's mischievous explorations were driven by his need to better understand the world around him. The victims of these inquiries were the record players, televisions, and on one memorable occasion, his mother's washing machine, which were disassembled in the name of science. Adam's love for physics was awakened when he entered high school. He attributes this to his first physics teacher, Louis Love. Adam describes Mr. Love as a teacher with great enthusiasm whose excitement in demonstrating concepts and ideas would draw him into the subject.

After high school Adam went to the State University of New York at Albany. SUNY Albany shared a 3-2 program with Rensellaer Polytechnic Institute, which is located a short distance up the Hudson river in New York. Adam took 3 years of physics at Albany and his last 2 years at RPI, where he studied electrical engineering.

Adam's early research interests were driven by his love of computers. Adam's father appreciated Adam's nascent interest and motivated him by offering to buy him a computer if Adam would do a report on Einstein's famous $E=mc^2$ formula. For the first time in his life Adam ran to the library to do homework. It was only natural that as Adam sought out research opportunities in college, he was drawn to computer related work.

While at Albany, Adam chose to work in the lab of A.Kaloyeros, a professor that was working on chemical vapor deposition, a technique for fabricating computer chips. Adam's desire to work with computers also motivated his course of study at RPI. His intention was to enter the field of VLSI design (very large scale integration), which is the theory behind the design of computer chips. As his studies progressed, Adam began to realize that the possibility of contributing creative, innovative research in this field was limited, as computers largely design themselves, and the positions available to a young engineer would not lead towards research. The consequence of this realization is that Adam felt that to develop new and creative ideas, which was his specialty, he would need to change tracks.



Adam Wax

With the guidance of his father, Adam decided to continue on to graduate school at Duke University. Adam is extremely proud of his parents and attributes his success to the disciplinary example set by his father and the cultural influence of his mother. Adam states that his father is a self-made, successful businessman. He feels that his father's influence played a great part in his own work ethics.

In graduate school, Adam entertained the idea of studying high-energy physics, as he had enjoyed and excelled at quantum mechanics at RPI. However, in the middle of his first year, unexpected news made Adam lose interest in high-energy physics: funding for the super-conducting supercollider in Texas was terminated. As this was to be a source of future jobs and research in the high-energy field, Adam reconsidered and decided to study lasers instead.

Adam went back to his interests in computers again. The next logical step was the incorporation of optical technology into computing. Adam felt that knowledge of lasers was a skill that he needed to acquire. The only problem was convincing his future advisor, Professor John Thomas at Duke University, to take him on as a graduate student. Since Adam had come from an engineering background, his initial progress in Physics graduate school was not as rapid as some of the other students. But Adam was determined, and he persevered until

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✹ **THE SPECTROGRAPH**

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✹ GEORGE R. HARRISON SPECTROSCOPY LABORATORY

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The Spectroscopy Laboratory houses two laser research resource facilities. The MIT Laser Research Facility, supported by the National Science Foundation, provides shared facilities for core researchers to carry out basic laser research in the physical sciences. The MIT Laser Biomedical Research Center, a National Institutes of Health Biomedical Research Technology Center, is a resource center for laser biomedical studies. The LBRC supports core and collaborative research in technological research and development. In addition, it provides advanced laser instrumentation, along with technical and scientific support, free of charge to university, industrial and medical researchers for publishable research projects. Call or write for further information or to receive our Researcher's Guide, (617) 253-9774;**http://web.mit.edu/spectroscopy/www/**

Personalities... continued from page 2

Professor Thomas accepted him into his research group. Adam at first worked for him for free, supporting himself as a teaching assistant. He continued to do this until funding was secured for his project, which was using lasers for what was termed biomedical studies. He now recollects after doing biomedical research studies at the Spectroscopy Laboratory that his research at Duke was not so much biomedical but fundamental science studies. His thesis topic was the use of Wigner distributions to understand light propagation in turbid media. After a couple of preliminary studies were completed and published, Professor Thomas received an NIH grant based on the result of Adam's work. Thus ending his TA days!

Adam knew then that he wished to be a professor. He believes that just understanding a concept isn't really the same degree of knowledge as if you can convey that concept to others. Adam has had a fair amount of teaching experience. He has given talks at conferences and seminars. He developed an excellent public speaking style while teaching test preparation courses for the Princeton Review. Adam gave basic physics lectures 3 times a week, which helped him develop his teaching techniques. He feels that by becoming a professor, he is using his abilities to help people, especially since his research is in the biomedical optics field.

In 1998 Adam met Professor Michael Feld at a biomedical optics conference in Orlando. Professor Feld heard Adam talk and they got together and had some discussions about coherence. This topic was of interest to Professor Feld, since he currently had a student, Changhuei Yang, who was interested in studying the propagation of coherence through biological tissues. When Adam finished his thesis one year later, he wrote a letter to Professor Feld and asked whether he needed a postdoc. Professor Feld recognized Adam's talent and brought him to the Spectroscopy Laboratory. Under Professor Feld's guidance, Adam and Changhuei have collaborated on several successful research projects.

At MIT, Adam has used interferometry as a tool for cell biology studies to probe the structure, organization and dynamics of biological cells. This research is opening up new doors for the study of biophysical properties of the cell. Although several accomplishments have been made, Adam feels the research is still in an early stage. He has laid down the foundation for future research in the years to come.

Adam would like to thank Professor Feld for being a great mentor and for believing in him. He attributes much of his recent success in research to the role Professor Feld has played in his career. Adam would also like to acknowledge his wife, Jodi for her continued support and enthusiasm in all of his work. Adam has felt very fortunate to have the support of his father and mother and is most thankfully appreciative for this. This interviewer believes Adam Wax will be the type of professor that will share his excitement, love and enthusiasm for science and physics with all the students he encounters. ■

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"Measurement of Anomalous Phase Velocity of Ballistic Light in a random Medium Using a Novel

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(L1-L4, focal lengths f_1 - f_4) to permit the measurement of angular scattering distributions. The reference field is made to cross the detector plane at a variable angle by scanning lens L2 (f_2 = 4.5 cm) a distance *D*y perpendicular to the beam path. It can be shown using Fourier optics that this translation causes the reference field to be reproduced in the plane of the detector (D) with its angle of propagation changed by $q_T = 2\,Dy\,/f_2$ but its position unchanged. Figures 1(A) and (B) illustrate the effects of transversely scanning L2 in the imaging system using ray traces. It can be seen that light is collected at a specific angle relative to the exact backscattering direction [2]. In the current scheme, the maximum clear aperture permits angular scans over a total range of 480 mrad (27.5°). The angular resolution, q_{res} = 1.4 mrad (0.08°), is given by the diffraction angle of the 0.45 mm diameter collimated beam incident on the sample.

Figure 2(a) shows a typical a/LCI spectrum for interferometrically detected light, scattered by a monolayer of immortal epithelial cells (Figure 3). The square of the magnitude of the scattered field is plotted as a function of the scattering angle relative to the exact backscattering direction. The Fourier transform of this

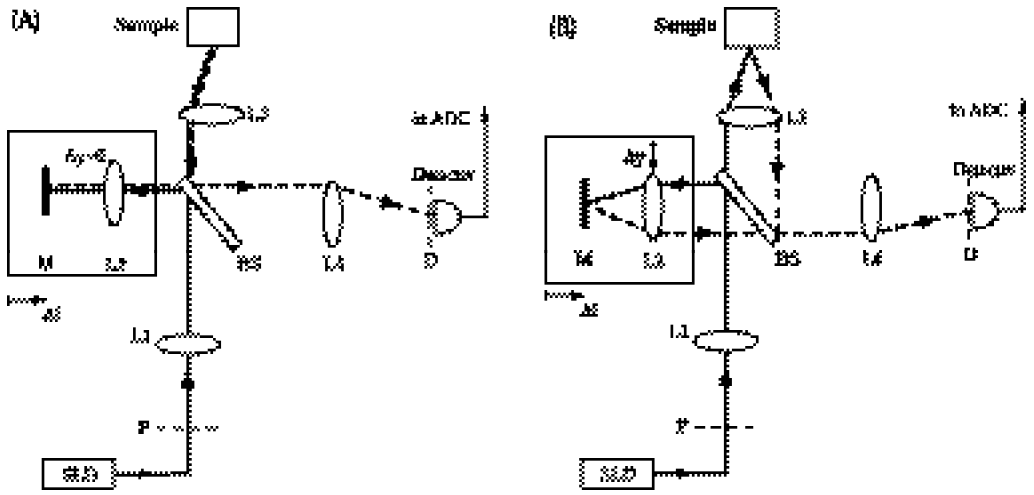

Figure 1: (a) Schematic of the a/LCI interferometer. (a) Detection of backscattered light. The photocurrent is digitized by an analog-to-digital converter and recorded using a PC. The distances between elements are: Plane P to L1 = 10 cm = f_1, L1 to BS = 10 cm, BS to L2 = 4.5 cm = f_2, L2 to M = 4.5 cm, BS to L3 = 4.5 cm = f_3, L3 to Sample = 4.5 cm, BS to L4 = 10 cm = f_4, L4 to Plane D = 10 cm. (b) Illustration of the displacement of lens L2 to vary the angle at which the reference beam crosses the detector plane.

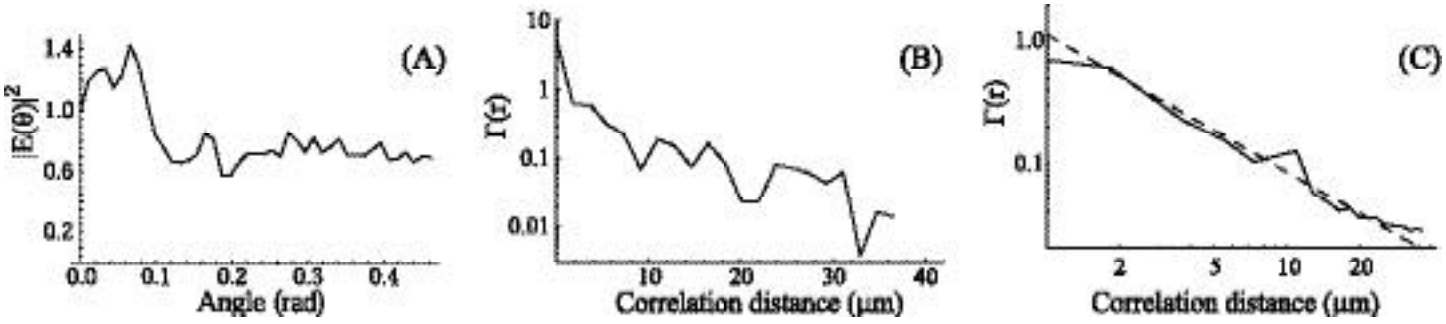

Figure 2: (a) Typical a/LCI spectra from HT29 epithelial cells. The spectra are shown as the mean square heterodyne signal as a function of scattering angle, relative to the exact backscattering direction. (b) Two-point correlation function Γr) of the scattering distribution shown in (a).(c) Correlation function for residual light scattering data. The data (solid line) are best fit by a power law (dashed line), indicating the self-similar nature of smaller structures within the model epithelial cells.

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data yields the two-point correlation function of the sample (Figure 2(b)). By comparing these data to various theoretical models [3, 4], we obtain structural and organizational information about the cell monolayer.

The size distribution of the cell nuclei is obtained by comparing the angular scattering distribution with the predictions of Mie theory. The structure of the cell nuclei was measured for twelve spatial points on the monolayer. The nuclei were found to have a mean refractive index difference of 1.066 +/- .007, a gaussian distribution of sizes with a mean diameter of 9.9 mm +/- 0.6 mm and a 1/e width of the distribution of 0.69 mm +/- 0.16 mm. In comparison, computer assisted image analysis of the photomicrograph of Fig. 3 yielded a mean diameter of 10.6 mm +/- 0.4 mm, and a 1/e width of the distribution of of 0.6 mm, both in good agreement with our a/LCI results

The a/LCI spectra can also be analyzed to obtain information about the organization of the sub-cellular structures. The Fourier transform of the a/LCI spectrum gives the two-point correlation function of the electric field scattered by the small structures, and thus describes their correlations. Figure 2(c) shows the two-point correlation function, $\Gamma(r)$, obtained by taking the Fourier transform of the residual distribution of the light scattering data shown in Figure 2(a), once the contribution of the nuclei has been removed. Remarkably, the straight line on this log-log plot clearly shows the inverse power law dependence of the correlations, indicating the fractal nature of the light scattering from sub-cellular structures. We find $\Gamma(r) \propto r^{-a}$, where for the twelve spatial points which are examined, the average correlation exponent, a = 1.21 +/- 0.10, corresponding to a fractal dimension, D = 1.79 +/- 0.10. The fractal dimension describes the way in which sub-cellular structures fill space within the cell. Further study is planned to examine the fractal dimension of cells at different stages of neoplastic transformation, and how changes in fractal dimension correlate with cell function.

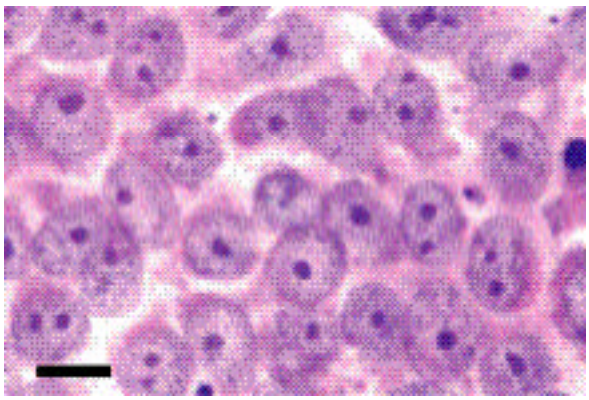

Figure 3: Photomicrograph of HT29 cell monolayer after fixation and staining. The length scale is indicated by the 10 μm bar. The large round objects are cell nuclei.The small dark spots within are nucleoli. Outlines of individual cells are diffuicult to see.

Phase-Referenced Interferometry

Another novel interferometric method we have developed is phase-referenced interferometry (PRI) (Figure 4), a method for measuring slow (~1–1000-nm/s) and small (~5-nm) cellular motion [5]. PRI achieves this great sensitivity and stability by the simultaneous use of two light sources: a cw 775-nm laser and a low coherence light source at 1550 nm. Movement within the target sample is measured with respect to a control interface on the sample that strongly reflects light at the cw wavelength. As the interferometer is used to probe the target sample, the signal at the cw wavelength is dominated by the control interface's reflection, with the low coherence interference signal arising from the selected interface(such as a cell membrane) within the sample. As the selected interface moves with respect to the control interface, the phase of the interference signal, ψ_{LC}, will shift with respect to that of the cw interference signal, ψ_{CW}. Specifically, the phase difference ψ_D is directly proportional to the optical path difference $n_{LC}L$, between the two interfaces:

$$\psi_D = \psi_{CW} - 2\psi_{LC} = \mathrm{mod}_{2\pi}(4k_{LC}n_{LC}L) \quad . \qquad (1)$$

Using this method of phase subtraction suppresses noise that arises due to interferometer jitter, the typical source of noise in phase measurement interferometry experiments.

We have demonstrated the ability of the method to study cellular movement non-destructively by applying it to measure the reaction of cell volume to hypotonic and hypertonic environmental changes (Figure 4). In this case, the sample consisted of cell monolayers grown on cover slips; the exposed side of the cover slip served as the control interface, and the membrane surface on the top of the cell monolayer was the target measurement interface. By focusing to a small spot (17mm wide), we targeted only a few (approximately three) cells. Upon abruptly changed the buffer's

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Lester Wolfe Workshop in Laser Biomedicine

Looking at the Brain Optically

Tuesday, May 14, 2002 4:00-6:30 PM

Massachusetts General Hospital
Wellman Laboratories of Photomedicine
Wellman 1 Conference Room
55 Blossom Street, Boston

From Single Neurons to Brains: In the Big Picture Do the Details Matter?
Matthew Wilson, Department of Brain and Cognitive Sciences, MIT

Optical Tomography and Functional Measurements
Britton Chance, Department of Biochemistry and Biophysics, University of Pennsylvania

***In vivo* Optical Imaging of Neocortical Epilepsy**
Theodore H. Schwartz, Weill Medical College of Cornell University/NYPresbyterian Hospital

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Refreshments served at 3:30 PM

Sponsored by G.R. Harrison Spectroscopy Laboratory, MIT
MGH Wellman Laboratories,
Harvard-MIT Division of Health Sciences and Technology,
and Center for the Integration of Medicine and Innovative Technology

PLEASE POST

Seminar on

MODERN OPTICS AND SPECTROSCOPY

Spring Semester 2002

February 26	Ken Shimizu and Vikram Sundar, MIT **Semiconductor Nanocrystals: From Single Dots to Lasing Dots**
March 5	Enrico Gratton, University of Illinois **Fluorescence Correlation Spectroscopy in Living Cells**
March 12	Fleming Crim, University of Wisconsin **Spectroscopy and Vibrationally Controlled Nonadiabatic Dissociation Dynamics of Ammonia**
March 19	Takeshi Oka, University of Chicago **Spectroscopy of H_3^+ in Laboratory and Astrophysical Plasmas**
April 2	Charles Shmuttenmaer, Yale University **Optical Pump THz Probe Spectroscopy: New Insights into Chemistry and Materials**
April 9	Patrick Vaccaro, Yale University **Nonlinear Spectroscopic Probes of Proton Transfer and Hydrogen Bonding in Model Organic Systems**
April 23	**Eleventh Annual Richard C. Lord Lecture** **Norman Ramsey**, Harvard University **Atomic Clocks**
April 30	George Barbastathis, MIT **Resonant Holography**
May 7	Arjun Yodh, University of Pennsylvannia **Imaging and Spectroscopy with Diffusing Light**
May 14	David Britt, University of California **New Insights into the Photosystem II Oxygen Evolving Complex via Pulsed EPR Spectroscopy**

TUESDAYS, 12:00-1:00, Grier Room (34-401)
Refreshments served following the seminar
Sponsored by the George R. Harrison Spectroscopy Laboratory and the School of Science, MIT, and the Rowland Institute for Science

PLEASE POST

Trace Explosives Detection Using Cavity Ringdown Spectroscopy

M. Hunter, S. Coy and J. I. Steinfeld
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J. T. Arnold
Varian Medical Systems, Ginzton Technology Center
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Introduction On December 21 1988, Pan Am flight 103 crashed over Lockerbie, Scotland, as a result of a terrorist bomb explosion, killing all 259 people on board and 11 on the ground. The tragedy prompted the US Federal Aviation Administration (FAA) and Congress to intensify efforts for improving security measures at airports and passenger airline flights. Since that time, the Steinfeld group has been actively pursuing the application of various spectroscopic techniques to the detection of trace explosives vapors. The sense of immediacy of this work has become even more pronounced after the events of September 11 2001. In this article, we describe a prototype laser spectrometer which we are currently building in conjunction with BlueLeaf Networks Inc., for improving the capability of explosives detection systems at airports.

Optical spectroscopy is an attractive option for trace vapor detection for several reasons. The fact that molecules absorb light at distinct, characteristic wavelengths allows for the unique spectral identification of a chemical by measuring the patterns of absorption observed when light passes through a sample. Compounds in a mixture can be differentiated on the basis of their spectroscopic signatures, if necessary with the aid of pattern recognition algorithms. Thus, optical spectroscopy has the potential to be useful for real-time detection and identification of vapor-borne samples of explosives, drugs, chemical agents and environmental contaminants, among others.

Traditional optical spectroscopic techniques, however, present severe limitations in terms of sensitivity when it comes to compounds with small molecular absorption cross sections or for more refractory compounds that have low equilibrium vapor pressures (corresponding to atmospheric mixing ratios of one part per billion (ppb) or less). In the case of low vapor pressure explosives such as cyclotrimethylene trinitramine (RDX), or pentaerythritol tetranitrate (PETN), their vapor (6.0 parts per trillion (ppt) and 18 ppt, respectively) would be difficult to detect under normal conditions using traditional optical spectroscopic methods.

Our groups at MIT and BlueLeaf Networks, Inc. are utilizing a new spectroscopic technique, Infrared Cavity Ringdown Spectroscopy (IR CRDS), which will improve the sensitivity and detection limits of explosive vapors over traditional optical spectroscopic techniques by several orders of magnitude. The instrument will couple a CRDS-based detector to an air sampling system comprised of a vapor separator/preconcentrator that can increase the concentration of the molecules of interest by a factor of 100 over a 10s collection period. This will enable the detection of molecules at ambient concentrations of 10 ppt by volume, which is sufficient to detect the equilibrium vapor pressure of many solid explosives at room temperature. Additionally, the vapor separator/preconcentrator will aid in the exclusion of other molecules present in ambient air that may interfere with the IR absorption of the explosives.

Cavity Ringdown Spectroscopy CRDS is based on the principle that when a pulse of light is injected into an optical cavity formed by highly reflective mirrors, the pulse will circulate within the cavity and the output of the cavity will decay exponentially with time (Figure 1).

The decay rate of the circulating intensity within the cavity is dependent on losses at the mirrors (due to their imperfect reflectivity) and attenuation by any absorber in the cavity. Since the mirror reflectivity is known (either through an empty cavity measurement, or a measurement made off-resonance to any absorbers present in the cavity), measuring the exponential decay allows us to detect the absorber in the cavity according to the following equation:

$$\text{decayrate} = \frac{1}{\tau} = \frac{c}{L}\left(\ln|R| + \alpha L\right),$$

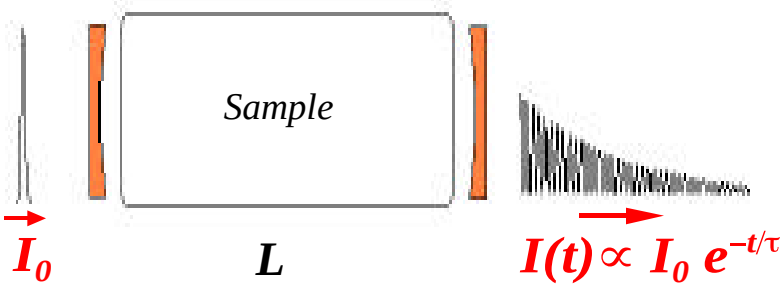

Figure 1. Schematic representation of a simple CRDS experiment

where τ is the measured exponential decay half-life (ringdown time) of the CRDS signal; α is the net absorbance of the analyte molecule; L is the length of the cavity; c is the speed of light, and is R is the reflectivity of the cavity mirrors.

One critical requirement for CRDS is the use of sufficiently high reflectivity mirrors, typically with R >99.99%. If such a highly reflective cavity is formed, then the light injected into the cavity can make up to 10^4 round trip passes, which translates into an effective absorption path length of tens of kilometers for typical cavity lengths on the order of 1m. Since absorption signals are directly proportional to the path length of the sample, this technique is thus capable of detecting an absorbance due to a very low sample density. It has been demonstrated that CRDS can detect absorption signals as small as 10^{-10} absorbance units, which is six orders of magnitude more sensitive than commercial absorption spectrometers.

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Experimental Setup The heart of our prototype instrument is a novel, tunable mid-infrared laser source consisting of an Er,Cr:YSGG – pumped ZGP Optical Parametric Oscillator (OPO) system. The ZGP OPO provides infrared laser pulses with an energy of 200 – 300 μJ/pulse; continuous tunability of the idler output beam is attained between 6 and 8 μm, with conversion efficiency > 10 %, by rotation of the ZGP crystal. The beam divergence is 6.2 mrad (excellent for OPO standards), and the OPO linewidth is 2.3 cm^{-1}. A schematic diagram of the laser system is shown in Figure 2.

The other critical component of our system is the set of high-reflectivity mirrors used in the CRDS cell. The data presented in this report was obtained with cavity mirrors of peak reflectivity *R*=99.993% at λ = 7.4-7.5 μm, corresponding to the absorption maximum of the $-NO_2$ symmetric stretch in the TNT molecule. The reflectivity remains *R*>99.98% over a ± 0.5μm range around this central region, allowing us to record vapor-phase absorption spectra in the wavelength range λ=7-8 μm. A second set of cavity mirrors, optimized for operation in the λ=6-7 μm region, can be used to scan over the $-NO_2$ antisymmetric stretch band.

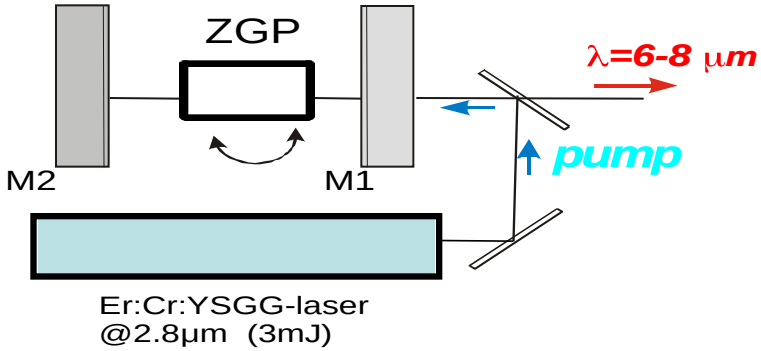

Figure 2. Schematic representation of tunable OPO laser system.

Current and Future Research Goals The detection limit expected for the CRDS system under development can be readily estimated from known absorption cross sections and saturated vapor pressures of the target molecules. For TNT, the room temperature saturated vapor density is 1.90 x 10^{11} molecules/cm^3, corresponding to 7.7 ppb by volume. The peak absorption cross section σ (6.41 μm) is 1.15 x 10^{-18} cm^2/molecule, giving an absorbance of 2.2 x 10^{-7} cm^{-1}, or δα = 2.2 x 10^{-6} for a single pass through a 10 cm cell. CRDS enhancement of the absorption signal, however, can further improve this sensitivity by several orders of magnitude. Our mirrors, with *R* >99.99%, provide typical ringdown times on the order of τ =20μs in the CRDS cavity, corresponding to $\alpha_{min} = 1/c\tau \sim 2 \times 10^{-6}$ cm^{-1}. Since τ can be measured with 1% accuracy, the minimum detectable absorption becomes $\delta\alpha_{min} = (\delta\tau/\tau)\,\alpha_{min} \sim 2 \times 10^{-8}$ cm^{-1}. With an additional 100-fold increase in vapor density, attained via preconcentration, our system will then be amply suited for detection of TNT well below its saturated vapor pressure, and will also be capable of detecting the less volatile compounds RDX and PETN.

Experimental tests of our CRDS system sensitivity have been performed by placing explosives samples directly into the CRDS cell, thereby collecting absorbance signals under equilibrium vapor pressure conditions (i.e., without sample preconcentration). Figure 3 shows the CRDS spectra of TNT obtained in this manner, in the temperature range T=25-60 °C. A signal-to-noise ratio of 10 was obtained for room temperature TNT detection at λ = 7.41 μm, with a 3s integration time, in good agreement with the estimate presented above.

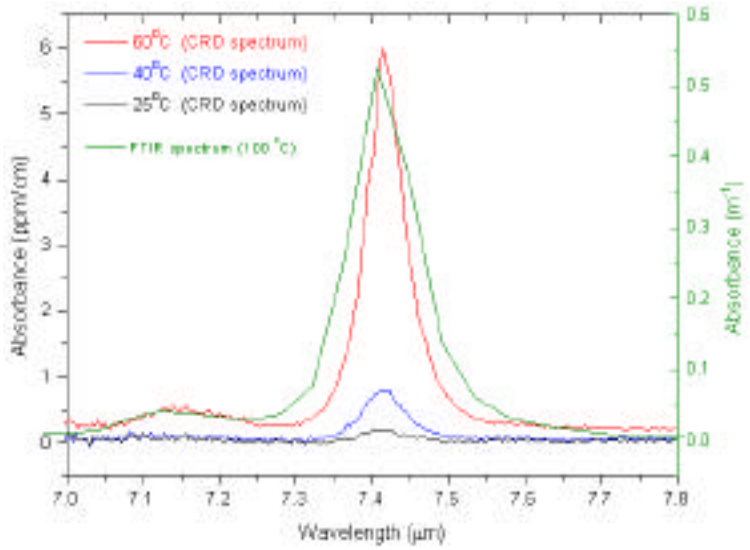

Figure 3. CRDS spectra of TNT at T=25-60 °C.

Future work will include addition of a membrane separator and a preconcentrator system in order to increase the concentration of explosive molecules and exclude some of the air components that could pose interferences in the absorption signal. A polydimethylsiloxane (PDMS) semi-permeable membrane will be used to provide a high level of partitioning of the target molecules from potentially interfering species such as water vapor and other small molecular contaminants usually present in air. Following membrane separation, an internal carrier stream of nitrogen will transport the sample through an accumulator which immobilizes the

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sample by collecting it onto a micro cold finger. In a cyclical process, the accumulator section can be flash-heated to release the accumulated sample into the CRDS optical cavity for spectroscopic analysis.

With such high sensitivity, trace amounts of interfering species passing through the membrane separator could interfere with the desired explosive vapor signal. Several species normally present in air exhibit strong absorptions in the IR region at which the target species absorb. Fortunately, intelligent pattern recognition can greatly increase the reliability of component identification and interpretation. The multi-spectral properties of the target molecules can be used as a unique signature to identify a specific compound. Work is currently under way to develop suitable algorithms to aid in this analysis.

Conclusion The CRDS system currently under development promises to vastly improve traditional optical techniques and advance the field of vapor detection. CRDS presents numerous advantages over traditional methods: significant improvement in sensitivity, especially when coupled to a membrane separator/preconcentrator system; increased specificity, largely due to the characteristic absorptions of a molecule; better stability, since shot-to-shot fluctuations in the laser pulse intensity do not affect the ringdown time; and last but not least, simplicity, since CRDS requires only a few basic optical components to operate. With these advantages, we are under way to develop a prototype CRDS instrument that will be useful in real world applications of explosives detection.

Reference Further details on detection techniques for explosive vapors, with extensive references to the literature, may be found in the review by J. I. Steinfeld and J. Wormhoudt, *Annu. Rev. Phys. Chem.* 49: 203-232 (1998).

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suspected threats. Metal detectors used for screening airline passengers, for example, have been a great deterrent to the gun-point hijacking of airplanes more prevalent in the past - and I am glad for it. Life is sacred, and should be protected whenever possible. In today's world of airline security, the focus has changed to screening for plastic explosives, such as those involved in the collapse of PanAm flight 103 in 1988, or in the more recently-averted "shoe-bomb" incident on a Paris-Miami American Airlines flight. The technique of spectroscopy is particularly well-suited for the detection of trace vapors, given its high sensitivity and inherent selectivity, and is therefore of potential benefit for screening of explosives compounds at airports. In fact, one of the research articles in this newsletter describes current efforts in Prof. Jeffrey Steinfeld's group to develop such an instrument for the Federal Aviation Administration.

However, on a deeper level, preventive measures alone cannot resolve a vulnerability to terrorist acts. From a technological standpoint, first of all, it is implausible to expect the implementation of a fool-proof system capable of protection against any and all possible terrorist attacks. A similar debate has been heard in the past, in relation to the proposed Star Wars Missile Defense plan proposed by the Reagan Administration, with a resounding conclusion from the scientific community against the technological feasability of such a scheme. The problem is greatly compounded in the present by nature of the multi-varied aspect of the possible terrorist attacks the nation faces - including chemical, biological, explosives and nuclear threats.

In addition to the technological issues, one must also consider the human dimension of the problem. People who perpetrate crime should clearly be held responsible for their acts. However, justice must be pursued fairly and consistently, with full due process granted to the accused. To make exception to this, relying instead on arbitrary use of power over individuals, may temporarily mitigate a particular terrorist threat, but it will also curtail lasting peace by planting further seeds of violence and hatred. In its highest form, bringing a person to justice involves dialogue - and so does peace. Let us not be afraid to meet that task, and let the world conscience be the true mediator and judge of affairs.

These issues are eloquently and succinctly summarized in a statement recently signed by 108 Nobel Laureates, who declared that:

"It is time to turn our backs on the unilateral search for security, in which we seek to shelter behind walls ... To survive in the world we have transformed we must learn to think in a new way. As never before, the future of each depends on the good of all." Technology - spectroscopy, in our case - is what we know, what we're good at, and what we're proud of (with good reason). However, it seems clear that the challenges we face today will require us to stretch ourselves beyond our familiar zones of discourse, knowledge and influence. This is no easy task, and it will require courage, commitment to our ideals, and the support and encouragement of a community with hope in a new destiny. Let's do it! ■



Martin Hunter

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osmolality to 85% (115%) of its normal value, the phase shift ψ_D associated with the cell membrane surface changed rapidly and then slowly recovered. In the hypotonic (hypertonic) case, the maximum change in cell thickness was approximately 0.2 mm (-1.3 mm) and took place over several hundred seconds. To our knowledge, this is the first time that cell volume changes of such small magnitude have been observed optically and continuously traced *in situ* for just a few cells.

We have also employed the method for elimination of interferometer jitter using harmonically related light sources to construct a novel phase dispersion microscope [6] and a novel phase-based optical tomographic system [7], both of which use dispersion for contrast. In addition, the technique allows observation of the subtle dependence on scatterer size of the phase velocity of ballistic photons that traverse a turbid medium [8]. Future applications of the PRI technique will study the characteristic motions of cells in response to various environmental stimuli, as well as search for hidden order in the apparently random metabolic motions of cells.

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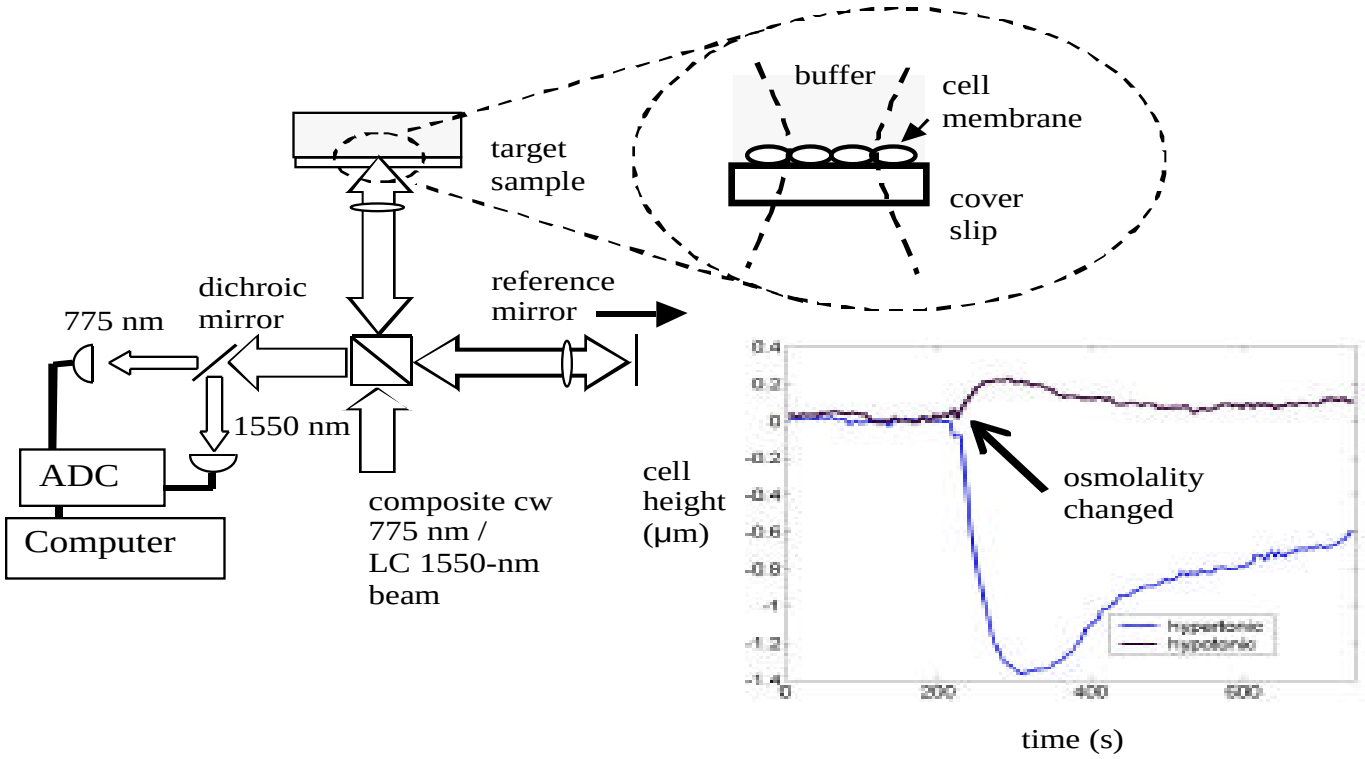

Figure 4: PRI setup and results of osmolality experiments.

✹ RECENT SPECTROSCOPY LABORATORY PUBLICATIONS

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