TERAHERTZ SPECTROSCOPY FOR MEDICAL INSTRUMENTATION DEVELOPMENT

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ABSTRACT

Recent development of sources and detectors in the THz regime (300 GHz to 3 THz) has enabled the precise measurement of material properties, including complex refractive indexes and loss tangents. Using our developed THz spectrometer, new data, in particular, of biological tissues has been used to develop potential THz medical imaging applications. In this paper, an overview of a 0.1-3 THz, with sub-GHz resolution spectroscopy system is presented that has been designed in particular to measure biological samples and provide data that will used to determine initial viability of THz medical imaging applications.

Keywords: Terahertz, photomixing, spectroscopy.

1. INTRODUCTION

Terahertz (THz) refers to the frequency range between radio frequency (RF) and far-infrared (FIR) electromagnetic radiation, typically defined as ranging from 300 GHz to 3 THz. Historically, it has been difficult to generate radiation in this frequency range. Due to slow carrier momentum relaxation times and other practical challenges, it has been problematic to produce semiconductor electronic devices that oscillate at these high frequencies. THz generation by photonic devices has also been difficult due in particular to the low photon energy. Recently, despite these challenges, several innovative techniques have been developed to generate THz radiation. Sensitive sources appropriate for many applications including imaging, have also been slow to develop and only in the last twenty years have enabling technologies been produced. Together these advances have enabled both THz spectroscopy and THz imaging.

With the technological advances, rich scientific information from many different materials, especially chemical and biological materials has been measured in the THz regime. In these materials, interatomic bonds, such as carbon-hydrogen bonds, have resonance frequencies in the far infrared (FIR). However, since many of these interatomic bonds are often universal in these materials, unique frequency signatures using FIR spectroscopy are uncommon. In contrast, the longer wavelength of THz waves resonate the intermolecular vibrational modes and rotational modes of short-chain molecular structures. These structures are unique in large, complex structures like DNA, RNA and proteins. Therefore, THz spectroscopy may provide distinguishable fingerprints of these materials possibly generating unique medical imaging applications.[1, 2]

The development of advanced and more sensitive THz spectrometers has enabled the measurement of the THz properties of materials including complex refractive indexes and loss tangents. These bear importance to chemical, biological and the medical sciences. The advances in sources and detectors at THz frequencies have also made THz medical imaging a possibility. Recent THz imaging applications being developed are the assessment of burns, the determination of corneal hydration and possible detection of skin cancer. While system engineers develop more robust, more sensitive imagers, often the optimal frequency of operation and bandwidth is difficult to determine due to scarcity of characterization data of biological tissues at THz frequencies. THz spectrometers are an invaluable tool to system engineers to guide design, and to develop the basic science for THz medical imaging. In this paper, a sub-GHz resolution, tunable spectroscopy system covering the full frequency range from 0.1 THz to 3 THz is used for initial determination of the viability of THz medical imaging applications. An overview of the system design and operation will be presented, followed by initial spectroscopy results of simple biological materials, lactose and biotin.

2. SUB-GHZ RESOLUTION THZ SPECTROMETER

Photomixing THz sources are tunable over a wide spectral range, from 0.1 THz to 3 THz, with spectral resolution that is limited only by the laser linewidth (<<100 MHz[3]). Although FTIRs also cover such spectral range, it is not able to realize the same resolution. The spectral resolution of a FTIR is related to the spatial delay and therefore needs extremely long path lengths, often impractical, to achieve the same resolution as frequency domain techniques. For example, to achieve 5 MHz frequency resolution (typical resolution of a photomixing based spectrometer), a FTIR needs a ~ 30m tunable path length, assuming no apodization. Meanwhile, the spectral resolutions of time-domain THz spectroscopy systems are limited as well by the spatial delay. Time-domain THz spectroscopy systems typically consist of a ZnTe nonlinear optical crystal and a bulky and expensive ultrafast Ti:Sapphire femtosecond laser and amplifier. In time-domain systems, the femtosecond pulse is used to sample the THz pulse within the nonlinear crystal by an optical delay line (i.e. electro-optic sampling). Beyond the practical difficulties in building the system, its spectral resolution is also limited by the length of the delay line.

Our THz spectrometer features a photomixing source to achieve sub-GHz frequency resolutions as well producing simpler and less costly system architecture. Our source in essence consist an antenna (Figure 1) coupled photomixer that is pumped by two tunable 780 nm continuous wave

(CW) lasers. The two CW laser beams illuminate the center gap of the antenna from which photocurrent is generated in the interdigitated fingers. A DC bias is applied through at ends of the spiral antenna to provide photoconductive gain. The photocarriers produced by the laser absorption of the two beams separately are too slow to respond to the instantaneous near infrared (NIR) electric field but fast enough to respond to the beat note of the two lasers. Therefore the photocarriers are driven by the beat note to generate an oscillating photocurrent at the beating frequency. In other words, if the two CW lasers are operating at the frequencies of ω_1 and ω_2, radiation at the difference frequency, $\Delta\omega = |\omega_1 - \omega_2|$ is generated by the photomixer and radiated through the antenna. Because the difference frequency, $\Delta\omega$, is much lower than the fundamental NIR (~780 nm) laser frequencies, this generation process is called optical rectification. To better couple the generated THz radiator from the antenna to free space and increase beam directivity, a silicon hyperhemispherical lens is attached to the backside of the photomixer semiconductor substrate.
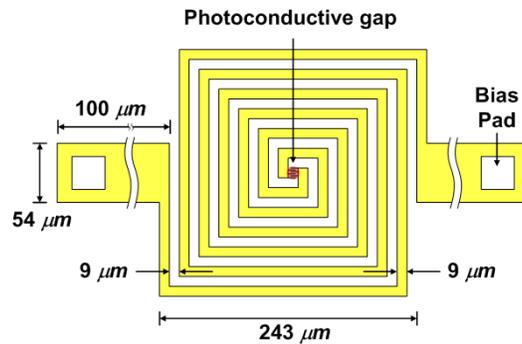

Figure 1: Diagram of the antenna coupled photomixer.

Our system (Figure 2) consists of a Distributed Feedback (DFB) diode laser kept fixed at 780 nm and a widely tunable, External Cavity diode laser (ECDL) that is tunable over +/- 10 nm range centered at ~780 nm. Both lasers generate 50 mW of optical power. The two laser beams are combined with a 50/50 beamsplitter, with one arm of the combination coupled into a wavemeter for precise frequency measurement, while the second arm is mechanically chopped at 16 Hz, and then focused onto the photomixer using y a 10x microscope objective. To be extremely flexible in measuring different samples, we built two different measuring configurations for transmission spectra (Figure 2b and 2c). Not shown, the system is also easily reconfigured to measure reflection spectra. The configuration of Figure 2b is designed to illuminate the sample with a large collimated beam so as to measure spectrum under certain uniform beam incident angle, while the configuration of Figure 2c is designed to focus the THz beam for use when the material being measured is highly attenuative.

Once the THz beam has passed through the sample, both configurations steer and focus the beam into a Golay Cell detector. The Golay cell, a commonly used THz detector due to high sensitivity, has a specific noise equivalent power spectral density (NEP) of 2×10^{-10} W/Hz$^{1/2}$ and with a built-in preamplifier, a responsivity of 10^4 V/W . The output electrical signal from the Golay cell is measured by a lock-in amplifier using the mechanical chopper as the reference frequency. The system using the focused configuration (Figure 2b), the average THz power was measured to be

0.2µW at low frequencies (100GHz ~ 200GHz), with a 10dB roll off at about 1 THz. The roll off is mainly due to the frequency dependent sensitivity roll off of the Golay cell detector.
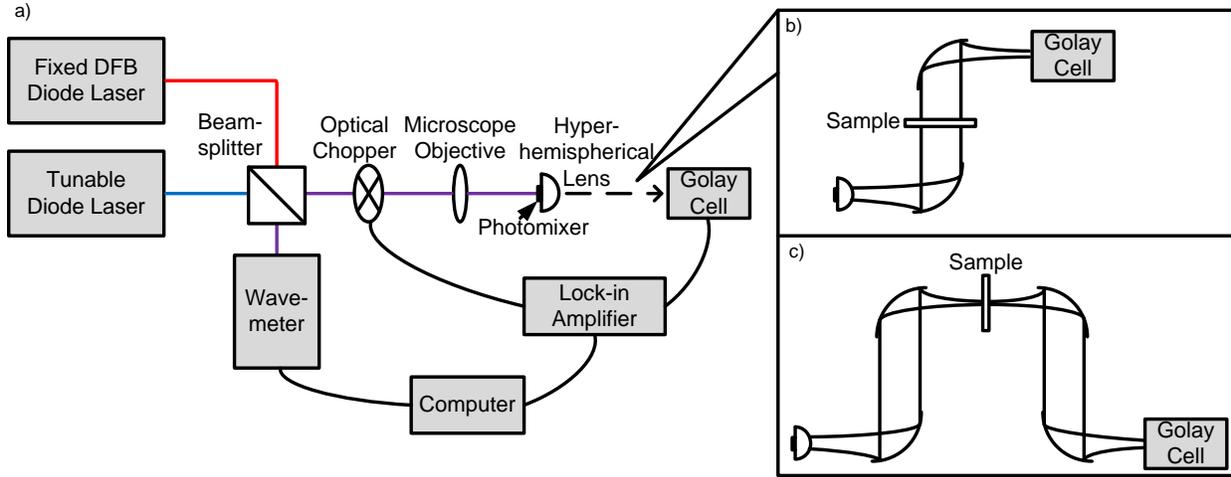

Figure 2: Block diagram of photomixing THz spectroscopic system.

3. EXPERIMENTAL RESULTS

3.1 Photomixing spectral resolution and waterlines

Water vapor is known as the most prevalent and strongest absorber of THz wave in the atmosphere and the THz absorption lines are often referred to as water lines. Since water lines are narrow, they provide a convenient and excellent benchmark for measuring the spectral resolution of a THz system. Using the configuration shown in Figure 2b, a total THz path length (from the photomixer to the Golay cell) of ~ 12 cm, and no sample in the beam path, an atmosphere spectrum was measured (i.e. water lines). The resulting spectrum is shown in **Figure 3**, in which the three strongest absorption lines (water lines) in this region are measured to be at 987 GHz, 1097 GHz, and 1162 GHz respectively. This is within ±0.2% of the data obtained from *HITRAN* database, which are 988.9 GHz, 1098.1 GHz and 1163.7 GHz respectively.
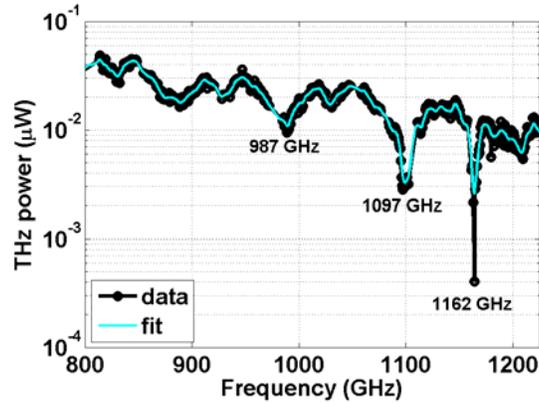
Figure 3: Experimental results of water vapor absorption. Three water lines are at 987 GHz, 1097 GHz and 1162 GHz respectively.

3.2 THz filter performance test with photomixing system

THz spectrometers are also useful to characterize system components such as filters. Filters of known specifications are especially convenient mean to verify operation. We tested four THz metal mesh filters, designed and manufactured by Virginia Diodes, Inc. (VDI)[4] using the configuration shown in Figure 2b, yielding a collimated THz beam incident perpendicularly onto the filter. The test results are shown in Figure 4. As we can see, as the center frequency of the mesh filter increases, their bandwidths also increases. This shows a good example of the importance of THz spectrometer in THz system components development.
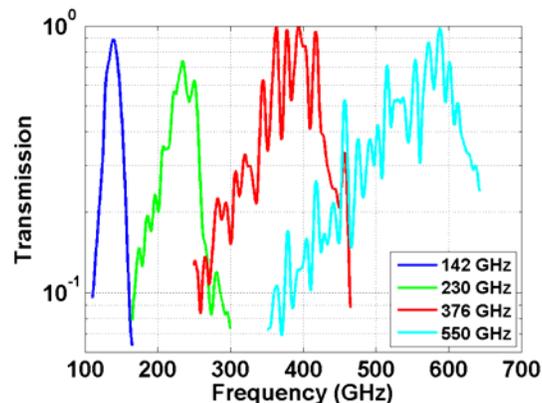

Figure 4: Experimental results of transmission of four THz metallic mesh filters.

3.3 Lactose and Biotin absorption spectrum in THz region

Lactose ($C_{12}H_{22}O_{11}$) and Biotin ($C_{10}H_{16}N_2O_3S$) are both organic solids, which are generally considered to have resonant absorption signature in THz region, due to optically active phonons. Lactose consists of a β-D-galactose ring bonded to an α/β-D-glucose ring through an oxygen linkage.[5, 6] Both solid-state Lactose and biotin were made by pressing Lactose powder and

Biotin powder so as to eliminate scattering from the powder particle. The structures of isolated-molecule and solid-state Lactose and Biotin are shown in Figure 5.[5] Also shown are the low frequency vibrational modes of both materials, including the twisting modes and bending modes. Experimental results of attenuation of both materials in solid-state conformation are shown in **Figure 6**. The two attenuation spectra showed great similarity. They both have large absorption signature at around 550 GHz and 1400 GHz. In the vicinity of 1100 GHz, they also both have absorption peak. Lactose has an absorption line at 1745 GHz, where the biotin spectrum is absent of corresponding absorption in the measured frequency range. It is also apparent that the lactose absorption lines are narrower than those of biotin.
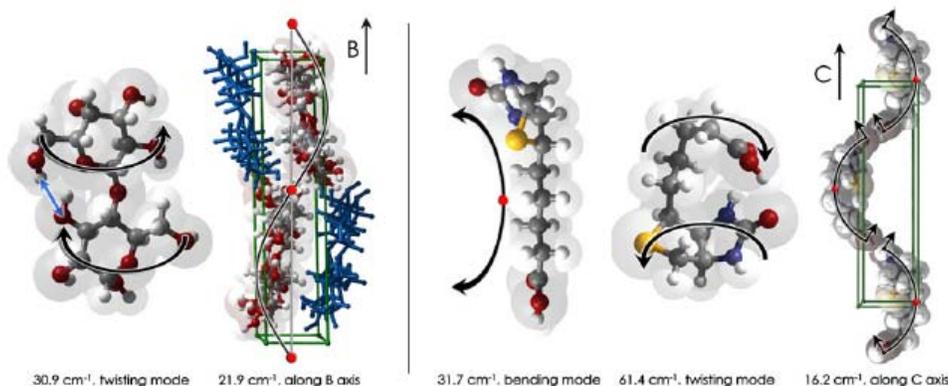

Figure 5: Structures of isolated-molecule and solid-state Lactose (left) and Biotin (right). Red dots indicate the hindered rotation solid-state axes and the blue double-headed arrow indicates the intramolecular hydrogen bond broken in the solid-state. The biotin solid-state mode is represented as a one-dimensional chain for clarity.[5]
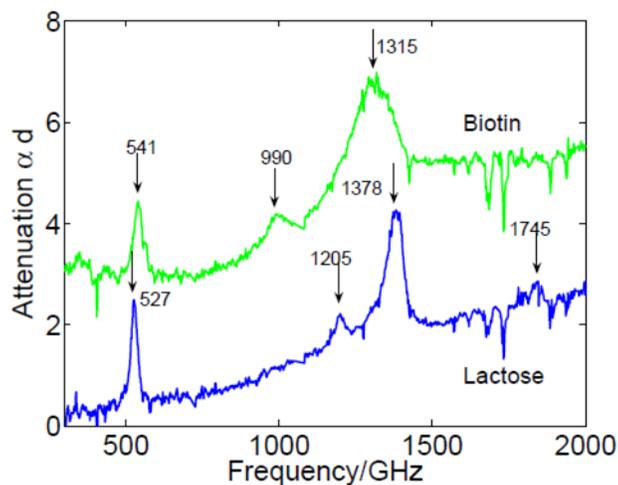

Figure 6: Attenuation of Biotin and Lactose. The Biotin data is shifted vertically to avoid overlap.

The spectrum results illustrate the measuring capabilities of biological samples, and show the potential of the spectrometer in designing imaging systems. Using the spectrometer and the characterization results obtained from the instrument, frequency dependent signatures of biological tissues can potentially be exploited for novel medical imaging applications. The spectrometer developed and presented will be used to indentify initial feasibility of potential medical applications.

4. CONCLUSION

The THz photomixing spectroscopic system presented covers the spectral range from 0.1 THz to 3 THz with sub-GHz spectral resolution. The system is an extremely powerful tool in THz research. It provides a direct tool in chemical and biological material THz spectroscopy study. Short-chain molecular structures showed strong and narrow absorption features in sub-THz region due to intermolecular vibrational modes. These absorption features may provide fingerprints of complex biological structures, which are extremely important in biological and medical research. While system engineers develop more robust, more sensitive imagers, the THz spectrometer developed will be used to determine the optimal frequency of operation and bandwidth and further characterization biological tissues at THz frequencies.

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