Terahertz Microchip for Illicit Drug Detection

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***Abstract*—To accurately detect minute amounts of substances without disturbing the surroundings of target molecules has been a major goal in bioanalytical technology. Here by integrating an optoelectronic terahertz (THz) microsource into a glass-substrated microchip within the near-field distance, we demonstrate a compact, label-free, noninvasive, and sensitive microbiosensing system with low-power consumption. The demonstrated THz microchip allows us to locally specify various illicit drug powders with weights of nanograms, with a promising future for rapid identification of the static status or even the dynamics of various biomolecules.**

***Index Terms*—Biochip, far-infrared, microchip, millimeter-wave, photonic transmitter, submillimeter wave, terahertz (THz).**

SENSING devices designed to identify minute amounts of biochemical substances accurately and noninvasively are strongly desired for many applications, such as in lab-on-a-chip development. Current analytic methods, including fluorescence-based techniques, require modification of the surroundings of molecules, thus disturbing the nature of the target molecules that could lower the precision of detection [1], [2]. One alternative without disturbance of target molecules is the terahertz (THz)-based biosensing technique [2]–[6]. Based on molecular fingerprints, direct THz-probing is a sensitive, label-free, and noninvasive way for biomolecule detection. It is thus highly desirable to directly integrate a THz microsource with the biochip system within the near-field distance for highly sensitive and localized detection of biomaterials in channels. Although applying THz technologies to lab-on-a-chip is beneficial, the challenge that the glass-substrate of most biochips is much absorptive at the THz range must be overcome. A high sensitivity THz sensing technique was demonstrated by Kurz's group, which used an integrated planar microwave waveguide based on microstrip line resonantors to detect the DNA binding state (as a function of refractive index) [2], [4]. However, modification of the deposited DNA on the planar waveguides is required. Moreover, the demonstrated system cannot be used repeatably and is less suitable for planar integration with a wide variety of currently available biochip modules.

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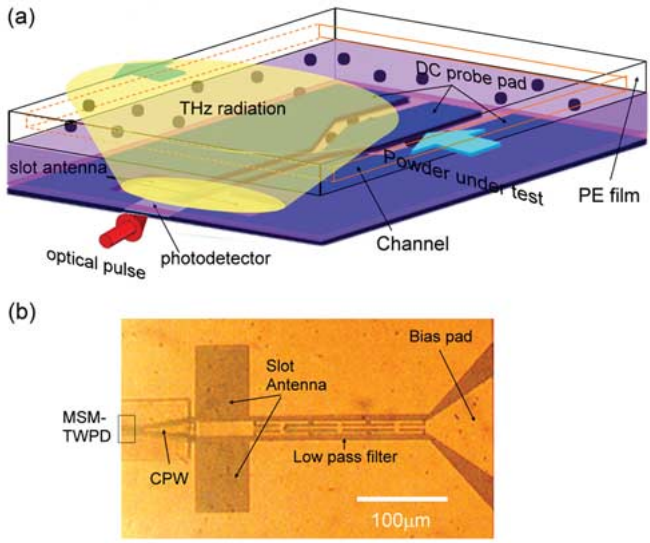

Fig. 1. (a) THz-integrated biosensing chip which is composed of a PE sample cell with microchannels therein, a 150-μm-thick glass substrate, and an integrated membrane-type THz photonic transmitter on the bottom of the glass substrate with a thickness of 5 μm. (b) Bottom view of the device showing the electronic circuit of the photonic transmitter [9].

In this letter, we demonstrate the feasibility to directly integrate an optoelectronic micro-THz source into a glass-substrated microchip for direct, sensitive, and localized sensing of biomolecules, which are preserved in their native states. Through optical control [7], the near-field THz absorption spectra of the molecules inside the microchip can be directly acquired while different biomolecules can be distinguished according to their THz fingerprints. With <5-mW optical power, the demonstrated system allows us to specify different illicit drug powders with weights of nanograms.

Fig. 1(a) illustrates the schematic diagram of the proposed THz-biosensing chip with a size of 1 mm $\times$ 1 mm. The top part is the glass-substrated polyethylene (PE) sample cell with hot-embossed [8] 20-μm-deep channels where sample powders were contained. The weights of the powders inside the detection channel were on the order of 300 ng, estimated by an area ratio method. A broadband THz photonic transmitter was inversely integrated in the bottom of the 150-μm-thick glass substrate. The layout of the photonic transmitter is shown in Fig. 1(b) [9]. The 5-μm-thick photonic transmitter is composed of an edge-coupled metal–semiconductor–metal traveling-wave photodetector (MSM TWPD), [10] coplanar-waveguides (CPWs), and a slot antenna [11], [12]. With an edge-coupled structure, illumination light with a THz beating frequency can be completely absorbed in the detector while high electrical bandwidth is preserved through a traveling-wave structure [13]. The light-driven

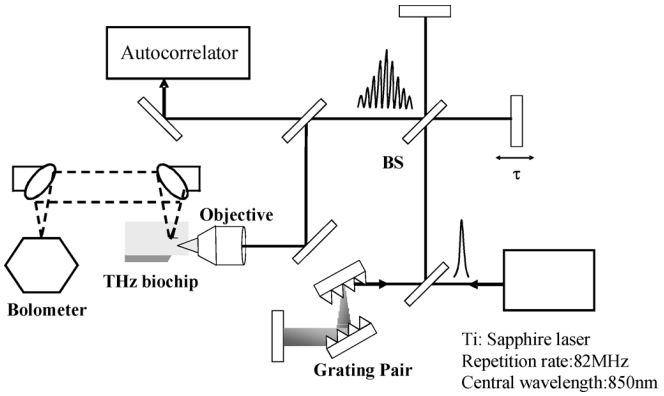

Fig. 2. Schematic diagram of the THz spectral measurement system. BS: beam splitter. Solid line: excitation beam. Dashed line: radiated quasi-CW THz beam.

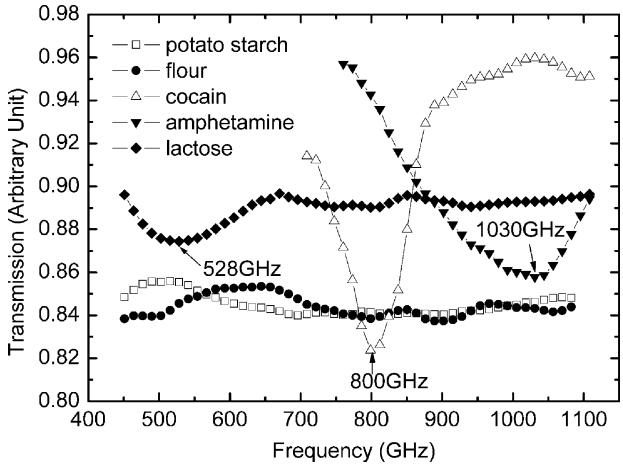

Fig. 3. THz microabsorption spectra of five different white powders tested, acquired by the THz microchip system. Two of them are illicit drugs including cocaine and amphetamine.

photocurrent output, with a THz frequency corresponding to the optical beating frequency, propagated through the CPW and fed into the slot dipole antenna for THz radiation. Through simulation (HFSS v10.0, Ansoft Company), the transverse electromagnetic (TEM) lines along the MSM TWPD and the CPW are confirmed to be well confined inside the glass, and have no effect on the tested powders. A wide tuning range from $<$100 GHz to 1.15 THz was demonstrated from a single photonic transmitter [9], while this glass-substrated device exhibited an exceptional high light-to-THz external power conversion efficiency of 0.33% [9]. Hence, under milliwatt average power optical excitation, the output average THz power after the highly absorptive glass was on the order of microwatts. By placing the microsample cell parallelly aligned right on top of the radiating slot antenna within a near-field distance of 150 μm, which is shorter than the THz wavelength, we are thus able to increase the THz photon flux at the samples as well as the percentage of the THz radiation experiencing the testing powders, achieving localized sensing with high sensitivity.

Fig. 2 shows the layout of the THz spectral measurement system, where we used a mode-locked Ti : sapphire laser and an optical coherent control system [7] for radiating frequency control. The grating pair stretched the 100-fs pulses at 800 nm with an 82-MHz repetition rate into linearly chirped pulses with a desired pulsewidth. By controlling the time delay of the two arms in a Michelson interferometer, we could control optical beating frequency [7], which is linearly proportional to the arm length difference. The beating light with an average power $<$5 mW was then focused into the MSM TWPD. The quasi-continuous-wave (CW) THz emission from the antenna, of which the radiation frequency and linewidth were controlled by the optical coherent control system [14], transmitting through the microsample cell in a THz near-field distance from the antenna, were collected by a pair of parabolic mirrors and a Si-bolometer for power detection. By inserting a chopper in the optical path and connecting the bolometer output to a lock-in, the background noise was reduced. We acquired the THz emission spectra (THz transmission intensity versus emission frequency) from the microchip with and without the tested powders by varying the optical beating frequency through the coherent control system. An HFSS simulation considering only the refractive index effect, neglecting the absorption constant of the tested powders, shows no significant (less than the system noise level) radiation power variation by adding different tested powders. Dividing the collected THz power with and without the samples at different frequencies, we thus acquired the THz absorption microspectrum of a specific drug powder, which directly reflects the vibrational nature of the tested molecules. Compared with the time-domain THz system, the spectral domain system is with a narrower emission bandwidth and thus with a higher spectral power density. The frequency domain system also possesses the unique characteristic that the acquired spectral range and resolution can be controlled, thus shortening the data acquisition time. With an optical pulsewidth of 10 ps and an excitation power of 4.8 mW, the signal-to-noise ratio (SNR) of the complete THz system was about 300 at 1 THz with a lock-in integration time of 100 ms. The SNR is better than 300 for the sub-THz regime. The obtained SNR can be further enhanced with higher optical excitation power, improved light-THz conversion efficiency, a longer integration time, or by shortening the distance between the microchip and the bolometer.

Fig. 3 shows the acquired THz absorption microspectra of five different white powders. With a finite scanning range and a reasonable spectral resolution (50 GHz in this specific case for faster scanning speed), the acquisition time of all traces can be within 1–5 s in our current system. With 300 ng of powders, the characteristic absorption peaks of cocaine (cocainae hydrochloridum, National Bureau of Controlled Drugs, Taiwan, R.O.C.) and amphetamine (methamphetamine, alpha-dimethylphenethylamine, National Bureau of Controlled Drugs, Taiwan, R.O.C.) at $\sim$800 [15] and $\sim$1030 GHz [15] can both be clearly identified, in sharp contrast to the potato starch, flour, and lactose powders. The latter has a 530-GHz [16] absorption peak. The low average transmission of potato starch and flour is due to the hexagonal molecular crystalline pattern which traps water molecules [17]. With the measured transmission variation, our system showed a 10-ng detection limit for cocaine and amphetamine powders under 4.8-mW excitation and with 100–ms integration time. The measurements were also repeated for stability test. High system stability can

be found. Taking amphetamine spectra as an example, the maximum frequency shift of the measured absorption peak was found to be one scan step (6 GHz for the trace in Fig. 3), which is much smaller than the frequency resolution of our system. This result indicates that our THz microchip system can provide the capability to identity different illicit drug powders with a minute amount (on the order of or less than 10 ng), which is with a sensitivity comparable to the current forensic toxicology identification techniques, such as fluorescence polarization immunoassay [18] and gas chromatography-mass spectrometry [19] with a detection limit of 100–500 ng/ml. With much improved sensitivity in the future, optoelectronic-integrated THz microchips should also enable water-based molecular sensing due to featureless and tolerable water absorption [20] through a 20- to 50-μm-thick microfluidic channel. With the detected molecules preserved in their original states, optoelectronic-integrated THz biochip should be able to provide the desired capability for future molecular dynamics studies.

In conclusion, we demonstrated the feasibility to integrate an optoelectronic-based micro-THz source with a glass-substrated microchip, with the sample in the near-field distance of the THz radiation antenna for localized biosensing. The capability to identity different illicit drug powders based on their spectral characteristics was successfully demonstrated with a <10 nanogram sensitivity. This THz microchip system has the advantages of label-free detection (need no probing molecules), high selectivity (based on spectral characteristics of molecules), no sample preparation, repeatable usage (just to replace the PE film), and ease of parallel integration with other biochip functionality modules, which are desirable for future lab-on-a-chip applications. In addition, by placing the detected molecules within the near-field distance of the micro-THz source, localized detection can be achieved, having the potential in multiplexing for future array applications. Our demonstration shows the possibility to integrate optoelectronic-based photonic transmitters with the current biochip technology for various biosensing applications, including DNA sequencing, explosive and virus detections. Due to the unique capability to detect the biomolecules in their natural states, the THz biochip should also enable future studies of molecular conformational dynamics.

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