

# Materials for terahertz science and technology

Terahertz spectroscopy systems use far-infrared radiation to extract molecular spectral information in an otherwise inaccessible portion of the electromagnetic spectrum. Materials research is an essential component of modern terahertz systems: novel, higher-power terahertz sources rely heavily on new materials such as quantum cascade structures. At the same time, terahertz spectroscopy and imaging provide a powerful tool for the characterization of a broad range of materials, including semiconductors and biomolecules.

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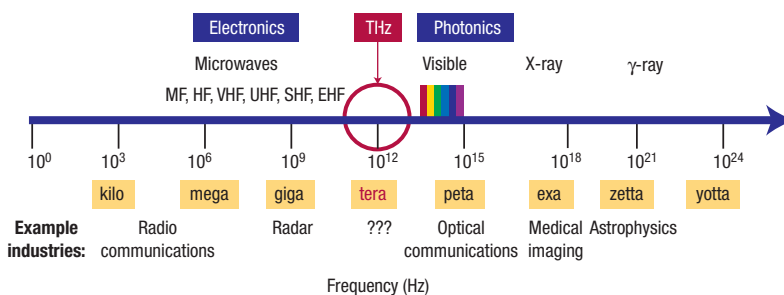
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Recent years have seen a plethora of significant advances in materials diagnostics by terahertz systems, as higher-power sources and more sensitive detectors open up a range of potential uses. Applications including semiconductor and high-temperature superconductor characterization, tomographic imaging, label-free genetic analysis, cellular level imaging and chemical and biological sensing have thrust terahertz research from relative obscurity into the limelight.

The terahertz (THz) region of the electromagnetic spectrum has proven to be one of the most elusive. Terahertz radiation is loosely defined by the frequency range of 0.1 to 10 THz ( $10^{12}$  cycles per second). Being situated between infrared light and microwave radiation (see Fig. 1), THz radiation is resistant to the techniques commonly employed in these well-established neighbouring bands. High atmospheric absorption constrained early interest and funding for THz science. Historically, the major use of THz spectroscopy has been by chemists and astronomers in the spectral characterization of the rotational and vibrational resonances and thermal-emission lines of simple molecules. The past 20 years have seen a revolution in THz systems, as advanced materials research provided new and higher-power sources, and the potential of THz for advanced physics research and commercial applications was demonstrated. Terahertz technology is an extremely attractive research field, with interest from sectors as diverse as the semiconductor, medical, manufacturing, space and defence industries. Several recent major technical advances have greatly extended the potential and profile of THz systems.



These advances include the development of a quantum cascade THz laser<sup>1</sup>, the demonstration of THz detection of single base-pair differences in femtomolar concentrations of DNA<sup>2</sup> and the investigation of the evolution of multiparticle charge interactions with THz spectroscopy<sup>3</sup>. This article provides an overview of these and many other important recent developments.

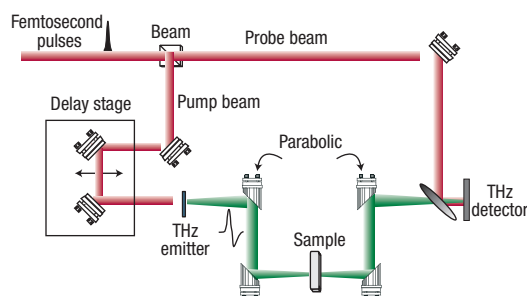
## THz SPECTROSCOPY SYSTEMS

Terahertz spectroscopy allows a material's far-infrared optical properties to be determined as a function of frequency. This information can yield insight into material characteristics for a wide range of applications. Many different methods exist for performing THz spectroscopy. Fourier transform spectroscopy (FTS) is perhaps the most common technique used for studying molecular resonances. It has the advantage of an extremely wide bandwidth, enabling material characterization from THz frequencies to well into the infrared. In FTS the sample is illuminated with a broadband thermal source such as an arc lamp or a SiC globar. The sample is placed in an optical interferometer system and the path length of one of the interferometer arms is scanned. A direct detector such as a helium-cooled bolometer is used to detect the interference signal. The Fourier transform of the signal then yields the power spectral density of the sample. One disadvantage of FTS is its limited spectral

**Figure 1** The electromagnetic spectrum. The development of efficient emitters and detectors within each of the spectral regimes has resulted in the birth of numerous industries. The search for potential applications of THz radiation is steadily intensifying as materials research provides improved sources and detectors.

**Figure 2** Illustration of a THz-TDS pump probe system.

The ultrafast laser beam is split into pump and probe beams. The pump beam is incident on the THz emitter to generate THz pulses, and the THz pulses are collimated and focused on the target using parabolic mirrors. After transmission through the target, the THz pulse is collimated and re-focused on the THz detector. The optical probe beam is used to gate the detector and measure the instantaneous THz electric field. A delay stage is used to offset the pump and probe beams and allow the THz temporal profile to be iteratively sampled.



resolution. Spectral measurements having a much higher resolution may be made using a narrowband system with a tunable THz source or detector. In these systems, the source or detector is tuned across the desired bandwidth and the sample's spectral response is measured directly. Both FTS and narrowband spectroscopy are also widely used in passive systems for monitoring thermal-emission lines of molecules, particularly in astronomy applications.

A third, more recent technique is termed THz time-domain spectroscopy (THz-TDS). THz-TDS uses short pulses of broadband THz radiation, which are typically generated using ultrafast laser pulses. This technique grew from work in the 1980s at AT&T Bell Labs and the IBM T.J. Watson Research Center<sup>4,5</sup>. Although the spectral resolution of THz-TDS is much coarser than narrowband techniques, and its spectral range significantly less than that of FTS, it has a number of advantages that have given rise to some important recent applications. The transmitted THz electric field is measured coherently, which provides both high sensitivity and time-resolved phase information. It is also amenable to implementation within an imaging system to yield rich spectroscopic images. A THz-TDS system is described in Fig. 2. Typical THz-TDS systems have a frequency bandwidth between 2 and 5 THz, a spectral resolution of 50 GHz, an acquisition time under one minute and a dynamic range of  $1 \times 10^5$  in electric field. Signal-processing algorithms may be used to improve the signal-to-noise ratio of the measured signals by almost 30% (ref. 6).

## THz SOURCES

The lack of a high-power, low-cost, portable room-temperature THz source is the most significant limitation of modern THz systems. However, there is a vast array of potential sources each with relative advantages, and advances in high-speed electronics, laser and materials research continue to provide new candidates. Sources may be broadly classified as either incoherent thermal sources, broadband pulsed ("T-ray") techniques or narrowband continuous-wave methods.

### BROADBAND THz SOURCES

Most broadband pulsed THz sources are based on the excitation of different materials with ultrashort laser pulses. A number of different mechanisms have been exploited to generate THz radiation, including photocarrier acceleration in photoconducting antennas,

second-order non-linear effects in electro-optic crystals, plasma oscillations<sup>7</sup> and electronic non-linear transmission lines<sup>8</sup>. Currently, conversion efficiencies in all of these sources are very low, and consequently, average THz beam powers tend to be in the nano- to microwatt range, whereas the average power of the femtosecond optical source is in the region of 1 W.

Photoconduction and optical rectification are two of the most common approaches for generating broadband pulsed THz beams. The photoconductive approach uses high-speed photoconductors as transient current sources for radiating antennas<sup>9</sup>. Typical photoconductors include high-resistivity GaAs, InP and radiation-damaged silicon wafers. Metallic electrodes are used to bias the photoconductive gap and form an antenna.

The physical mechanism for THz beam generation in photoconductive antennas begins with an ultrafast laser pulse (with a photon energy larger than the bandgap of the material  $h\nu \geq E_g$ ), which creates electron-hole pairs in the photoconductor. The free carriers then accelerate in the static bias field to form a transient photocurrent, and the fast, time-varying current radiates electromagnetic waves. Several material parameters affect the intensity and the bandwidth of the resultant THz radiation. For efficient THz radiation, it is desirable to have rapid photocurrent rise and decay times. Thus semiconductors with small effective electron masses such as InAs and InP are attractive. The maximum drift velocity is also an important material parameter, but it is generally limited by the intraband scattering rate or by intervalley scattering in direct semiconductors such as GaAs<sup>10-12</sup>. Because the radiating energy mainly comes from stored surface energy in the form of the static bias field, the THz radiation energy scales up with the bias and optical fluency<sup>13</sup>. The breakdown field of the material is another important parameter because this determines the maximum bias that may be applied. Photoconductive emitters are capable of relatively large average THz powers in excess of 40  $\mu$ W (ref. 14) and bandwidths as high as 4 THz (ref. 15).

Optical rectification is an alternative mechanism for pulsed THz generation, and is based on the inverse process of the electro-optic effect<sup>16</sup>. Again, femtosecond laser pulses are required, but in contrast to photoconducting elements where the optical beam functions as a trigger, the energy of the THz radiation in optical rectification comes directly from the exciting laser pulse. The conversion efficiency in optical rectification depends primarily on the material's non-linear coefficient and the phase-matching conditions.

This technique was first demonstrated for generating far-infrared radiation using LiNbO<sub>3</sub> (ref. 17). Much research has focused on optimizing THz generation through investigating the electro-optic properties of different materials, including traditional semiconductors such as GaAs and ZnTe, and organic crystals such as the ionic salt 4-dimethylamino-N-methylstilbazolium tosylate (DAST) among many others<sup>18-20</sup>. Because optical rectification relies on coupling of the incident optical power to THz frequencies at relatively low efficiency, it usually provides lower output powers than photoconductive

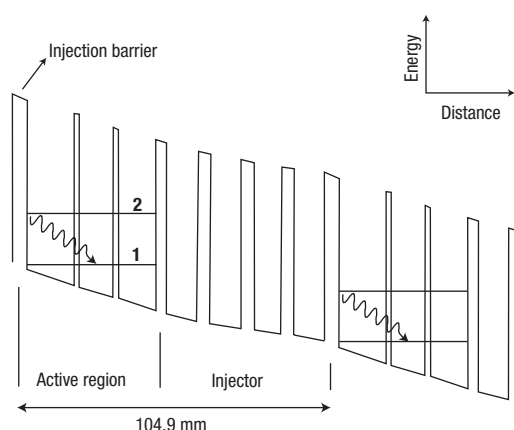
antennas, but it has the advantage of providing very high bandwidths, up to 50 THz (ref. 21). Phase-matched optical rectification in GaSe allows ultrabroadband THz pulses to be generated with a tunable centre wavelength. Tuning up to a frequency of 41 THz is accomplished by tilting the crystal about the horizontal axis perpendicular to the pump beam to modify the phase-matching conditions<sup>22,23</sup>.

## NARROWBAND THz SOURCES

Narrowband THz sources are crucial for high-resolution spectroscopy applications. They also have broad potential applications in telecommunications, and are particularly attractive for extremely high bandwidth intersatellite links. For these reasons there has been significant research interest in the development of narrowband sources over the past century<sup>24</sup>. A multitude of techniques are under development, including upconversion of electronic radio-frequency sources, downconversion of optical sources, lasers and backward-wave tubes. Several comprehensive reviews of this field are available<sup>25</sup>.

The technique most used for generating low-power (<100  $\mu$ W) continuous-wave THz radiation is through upconversion of lower-frequency microwave oscillators, such as voltage-controlled oscillators and dielectric-resonator oscillators. Upconversion is typically achieved using a chain of planar GaAs Schottky-diode multipliers. Using these methods, frequencies as high as 2.7 THz have been demonstrated<sup>26</sup>. Research also continues to increase the frequency of Gunn and IMPATT diodes to the lower reaches of the terahertz region using alternate semiconducting structures and improved fabrication techniques<sup>27</sup>. Gas lasers are another common THz source. In these sources, a carbon dioxide laser pumps a low-pressure gas cavity, which lases at the gas molecule's emission-line frequencies. These sources are not continuously tunable, and typically require large cavities and kilowatt power supplies, however they can provide high output powers up to 30 mW. Methanol and hydrogen cyanide lasers are the most popular, and they are in common use for spectroscopy and heterodyne receivers.

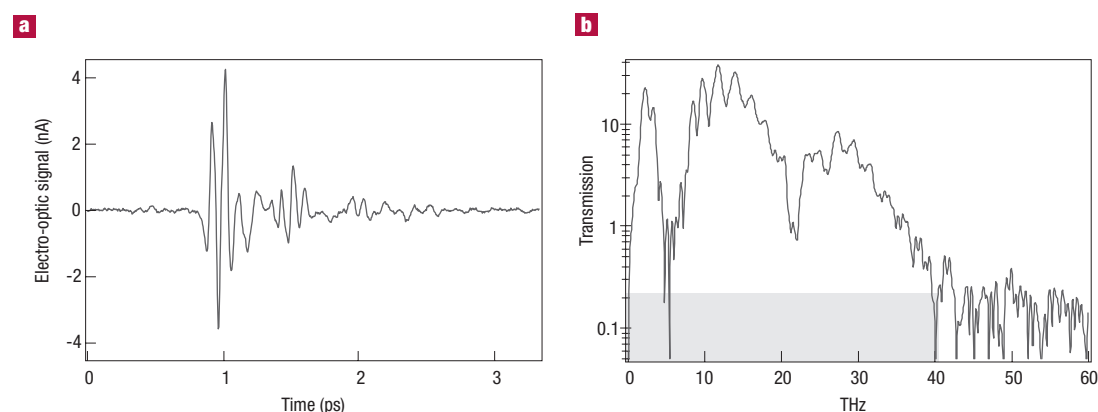
Extremely high-power THz emissions have recently been demonstrated using free-electron lasers with energy-recovering linear accelerators<sup>28</sup>. Free-electron



**Figure 3** Simplified conduction band structure of the THz quantum cascade laser demonstrated by Kohler *et al.* (after ref. 1). Electrons are injected through the 4.3-nm AlGaAs injection barrier into the level 2 energy state of the active region. The active transition from level 2 to level 1 results in the emission of 4.4-THz photons. The electrons then escape to the subsequent injector band. A total of 104 repeats of the basic 7 well structure was used in the laser. Each quantum well consists of a thin layer (10–20 nm) of GaAs between two potential barriers of AlGaAs (0.6–4.3 nm thick). The layer thicknesses and the applied electric field were tuned to provide the required tunnelling characteristics.

lasers use a beam of high-velocity bunches of electrons propagating in a vacuum through a strong, spatially varying magnetic field. The magnetic field causes the electron bunches to oscillate and emit photons. Mirrors are used to confine the photons to the electron beam line, which forms the gain medium for the laser. Such systems impose prohibitive cost and size constraints and typically require a dedicated facility. However, they may generate continuous or pulsed waves, and provide an average brightness of more than six orders of magnitude higher than typical photoconductive antenna emitters. Free-electron lasers have significant potential in applications where improved signal-to-noise ratio is essential, or in the investigation of non-linear THz spectroscopy. Bench-top variations on the same theme, termed backward-wave tubes or carcinotrons, are also capable of providing milliwatt output powers at THz frequencies, and are commercially available.

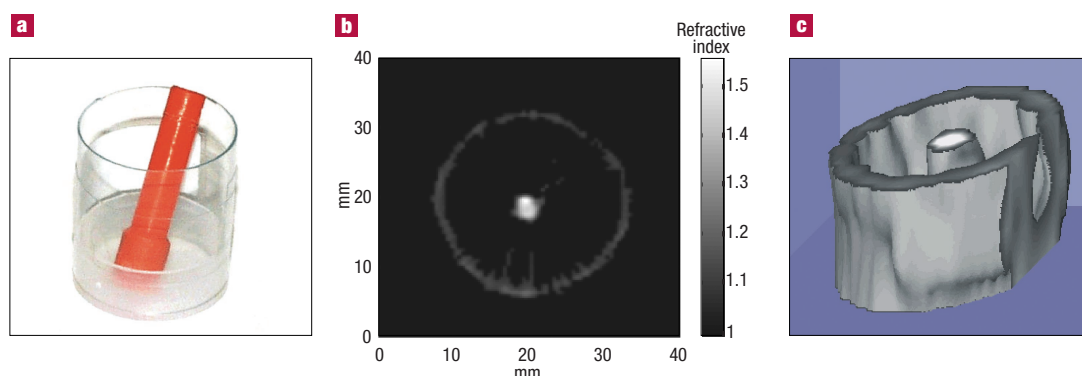
A number of optical techniques have also been pursued for generating narrowband THz radiation. Original efforts began in the 1970s using non-linear photomixing of two laser sources, but struggled with low conversion efficiencies<sup>29</sup>. In this technique, two continuous-wave lasers with slightly differing centre frequencies are combined in a material exhibiting a high second-order optical non-linearity such as DAST. The two laser frequencies mutually interfere in the



**Figure 4** A broadband THz pulse with a frequency spectrum extending into the infrared. **a**, Temporal waveform of a THz pulse generated using optical rectification in a 27- $\mu$ m ZnTe emitter, and measured using freespace electro-optic sampling in a 30- $\mu$ m ZnTe sensor. **b**, Frequency spectrum of the THz field. The absorption resonance at 5.3 THz is due to phonon modes in the ZnTe crystals.

**Figure 5** T-ray computed tomography image of two plastic cylinders (after ref. 57).

**a**, An optical image of the test structure. **b**, The target was imaged using the tomography system, and the refractive index of each cross-sectional slice was reconstructed. The central slice is shown. The greyscale intensity indicates the refractive index of the two different types of plastic. **c**, The cross-sectional slices are combined to form a 3D image. A surface-rendered image is shown.



material, resulting in output oscillations at the sum and difference of the laser frequencies. Such systems can be designed such that the difference term is in the THz range. Tunable continuous-wave THz radiation has been demonstrated by mixing two frequency-offset lasers in GaAs grown at low temperature<sup>30</sup> and by mixing two frequency modes from a single multimode laser. Further techniques use optical parametric generators and oscillators where a Q-switch Nd:YAG (neodymium:yttrium-aluminium-garnet) laser pump beam generates a second idler beam in a non-linear crystal, and the pump and idler signal beat to emit THz radiation<sup>31,32</sup>. Optical techniques provide broadly tunable THz radiation and are relatively compact owing to the availability of solid-state laser sources. Output powers in excess of 100 mW (pulsed) have been demonstrated<sup>33</sup>. Optical downconversion is a rich area for materials research because molecular beam epitaxy and other materials advances allows the generation of engineered materials with improved photomixing properties<sup>34</sup>.

Semiconductor lasers are a further technique with extreme promise for narrowband THz generation. The first such laser was demonstrated over 20 years ago in lightly doped p-type germanium as a result of hole population inversion induced by crossed electric and magnetic fields<sup>35</sup>. These lasers are tunable by adjusting the magnetic field or external stress. Terahertz lasing in germanium has also been demonstrated by applying a strong uniaxial stress to the crystal to induce the hole population inversion<sup>36</sup>. Such lasers have many inherent limitations including low efficiency, low output power and the need for cryogenic cooling to maintain lasing conditions. Recently, semiconductor deposition techniques have advanced to a level where the construction of multiple quantum-well semiconductor structures for laser emission is feasible. Quantum cascade lasers were first demonstrated in 1994 based on a series of coupled quantum wells constructed using molecular beam epitaxy<sup>37</sup>. A quantum cascade laser consists of coupled quantum wells (nanometre-thick layers of GaAs sandwiched between potential barriers of AlGaAs). The quantum cascade consists of a repeating structure in which each repeat unit is made up of an injector and an active region. In the active region a population inversion exists and electron transition to a lower energy level occurs, emitting photons at a specific wavelength. The electrons then tunnel between

quantum wells and the injector region couples them to the higher energy level in the active region of the subsequent repeat unit.

Quantum cascade lasers have been demonstrated within the infrared spectrum, but until very recently several significant problems had prevented THz quantum cascade lasers from being realized. The principal problems are caused by the long wavelength of THz radiation. This results in a large optical mode, which results in poor coupling between the small gain medium and the optical field, and in high optical losses owing to free electrons in the material (these losses scale as the square of the wavelength). Kohler *et al.*<sup>1</sup> addressed these and other problems in their recent innovative design of a THz quantum cascade laser operating at 4.4 THz. The laser consisted of 104 repetitions of the basic unit (shown in Fig. 3) and a total of over 700 quantum wells. This system demonstrated pulsed operation at a temperature of 10 K; however, optimized fabrication promises to lead to continuous-wave operation at liquid nitrogen temperatures (of the order of 70 K).

## THZ DETECTORS

The detection of THz-frequency signals is another area of important active research. The low output power of THz sources coupled with the relatively high levels of thermal background radiation in this spectral range has necessitated highly sensitive detection methods. For broadband detection, direct detectors based on thermal absorption are commonly used. Most of these require cooling to reduce thermal background. The most common systems are helium-cooled silicon, germanium and InSb bolometers. Pyroelectric infrared detectors may also be used at THz frequencies. Superconductor research has yielded extremely sensitive bolometers based on the change of state of a superconductor such as niobium. Interferometric techniques may be used to extract spectral information using direct detectors. A single photon detector for THz photons has recently been demonstrated<sup>38</sup>. This detector uses a single-electron transistor consisting of a quantum dot in a high magnetic field, to offer unparalleled sensitivity. Although detection speeds are currently limited to 1 ms, high-speed designs are proposed and this has the potential to revolutionize the field of THz detection.



In applications requiring very high spectral resolution of the sensor, heterodyne sensors are preferred. In these systems, a local oscillator source at the THz frequency of interest is mixed with the received signal. The downshifted signal is then amplified and measured. At room temperature semiconductor structures may be used. A planar Schottky-diode mixer has been operated successfully at 2.5 THz for sensing applications in space<sup>39</sup>. Cryogenic cooling is used for higher sensitivity in heterodyne superconductor detectors. Several superconductor structures have been used for over 20 years. The most widely used is the superconductor-insulator-superconductor tunnel junction mixer<sup>40</sup>. High-temperature superconductors such as YBCO (yttrium-barium-copper oxide) are touted for their potential for higher bandwidth operation. A number of general reviews of narrowband THz receivers are available<sup>41</sup>. Alternative narrowband detectors, such as electronic resonant detectors, based on the fundamental frequency of plasma waves in field-effect transistors have been demonstrated up to 600 GHz<sup>42</sup>.

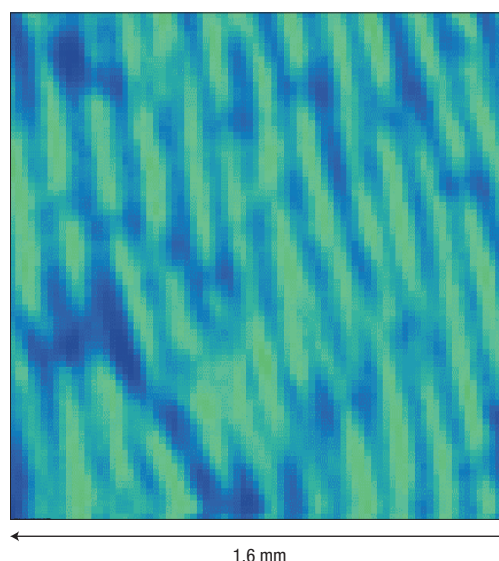
For pulsed THz detection in THz-TDS systems, coherent detectors are required. The two most common methods are based on photoconductive sampling and free-space electro-optic sampling, both of which again rely on ultrafast laser sources. Fundamentally, the electro-optic effect is a coupling between a low-frequency electric field (THz pulse) and a laser beam (optical pulse) in the sensor crystal. Simple tensor analysis indicates that using a  $\langle 110 \rangle$ -oriented zincblende crystal as a sensor provides the highest sensitivity. The THz electric field modulates the birefringence of the sensor crystal; this in turn modulates the polarization ellipticity of the optical probe beam passing through the crystal. The ellipticity modulation of the optical beam can then be analysed to provide information on both the amplitude and phase of the applied electric field<sup>43,44</sup>.

The use of an extremely short laser pulse ( $<15$  fs) and a thin sensor crystal ( $<30$   $\mu\text{m}$ ) allow electro-optic detection of signals into the mid-infrared range. Figure 4a shows a typical mid-infrared pulsed THz waveform. The Fourier transform of the THz pulse is shown in Fig. 4b; the highest frequency response reaches over 30 THz. The resonant absorption at 5.3 THz is caused by the phonon modes of the ZnTe crystals. When thin sensors are used, extremely high detection bandwidths, in excess of 100 THz, have been demonstrated<sup>45</sup>.

Photoconductive antennas are widely used for pulsed THz detection. An identical structure to the photoconductive antenna emitter may be used. Rather than applying a bias voltage to the electrodes of the antenna, a current amplifier and meter are used to measure a transient current. Ultrahigh bandwidth detection has been demonstrated using photoconductive antenna detectors with detectable frequencies in excess of 60 THz (ref. 46).

## THz APPLICATIONS

One of the primary motivations for the development of THz sources and spectroscopy systems is the potential to extract material characteristics that are unavailable when



**Figure 6** THz image of an onion cell membrane (after ref. 60). A THz imaging system based on optical rectification and free-space electro-optic sampling in ZnTe crystals 30  $\mu\text{m}$  thick was used with a bandwidth up to 40 THz. This allowed a spatial resolution of less than 50  $\mu\text{m}$  to be achieved. The cellular structure of the tissue membrane is clearly visible.

using other frequency bands. Astronomy and space research has been one of the strongest drivers for THz research because of the vast amount of information available concerning the presence of abundant molecules such as oxygen, water and carbon monoxide in stellar dust clouds, comets and planets<sup>47</sup>. In recent years, THz spectroscopy systems have been applied to a huge variety of materials both to aid the basic understanding of the material properties, and to demonstrate potential applications in sensing and diagnostics. We review several of the more recently demonstrated applications.

## MATERIAL CHARACTERIZATION

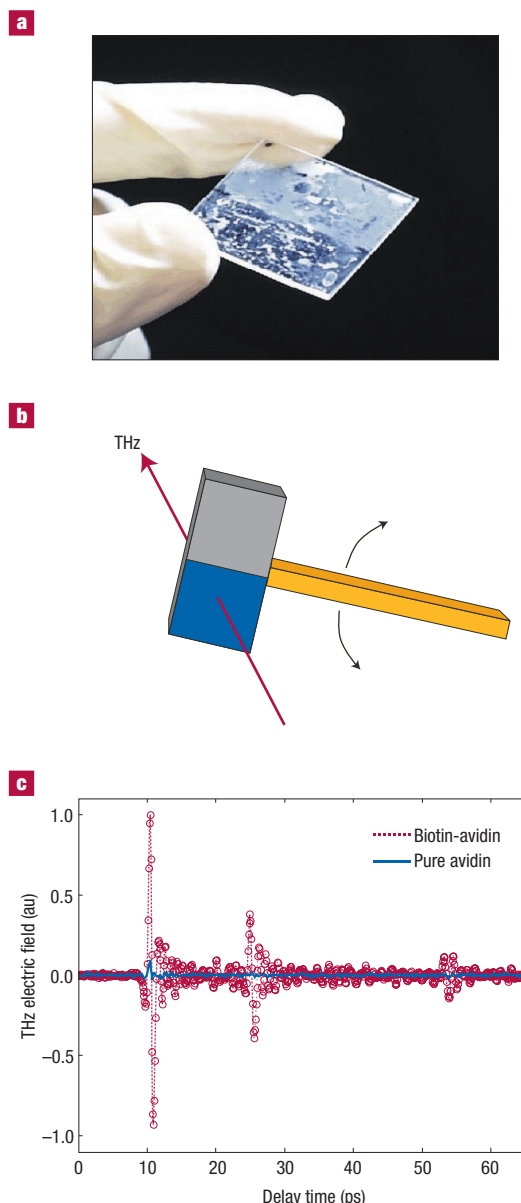
One of the major applications of THz spectroscopy systems is in material characterization, particularly of lightweight molecules and semiconductors. Terahertz spectroscopy has been used to determine the carrier concentration and mobility of doped semiconductors such as GaAs and silicon wafers<sup>48–50</sup>. The Drude model may then be used to link the frequency-dependent dielectric response to the material free-carrier dynamic properties, including the plasma angular frequency and the damping rate. An important focus is on the measurement of the dielectric constant of thin films<sup>51</sup>.

High-temperature superconductor characterization is another important application of THz spectroscopy. Several superconducting thin films have been analysed to determine material parameters including the magnetic penetration depth and the superconducting energy gap. THz-TDS has recently been used to study  $\text{MgB}_2$ , the material newly discovered to be superconducting. This material exhibits an extremely high transition temperature of 39 K and is currently not well understood. THz-TDS was used to determine the superconducting-gap energy threshold of approximately 5 meV. This corresponds to only half the value predicted by current theory and points to the existence of complex material interactions<sup>52</sup>.

Experiments with optical-pump THz-probe systems can reveal additional information about

**Figure 7** A biotin-avidin T-ray biosensor (after ref. 65).

**a**, The test slide consisting of a biotin thin-film, half coated with an avidin solution. **b**, Illustration of the measurement procedure where the slide is mounted on a galvanometric shaker and translated back and forth in the THz beam to allow the differential signal to be measured. **c**, The THz pulse measured after transmission through the biotin-avidin sensor with (dashed line) and without (solid line) exposure to  $0.3 \text{ ng cm}^{-2}$  of avidin molecules chemically bound to agarose beads in solution.



materials. In these experiments, the material is excited using an ultrafast optical pulse, and a THz pulse is used to probe the dynamic far-infrared optical properties of the excited material. Leitenstorfer *et al.* used an optical-pump THz-probe system to identify the time evolution of charge–charge interactions in an electron–hole plasma excited in GaAs using ultrafast optical pulses. This study added experimental evidence to quantum-kinetic theoretical predictions regarding charge build-up or dressed quasi-particles<sup>3</sup>.

#### THz IMAGING AND TOMOGRAPHY

Pulsed THz-wave imaging, or ‘T-ray imaging’, was first demonstrated by Hu and Nuss<sup>53</sup> in 1995, and since then has been used for imaging a wide variety of targets including semiconductors<sup>54</sup>, cancerous tissue<sup>55</sup> and flames<sup>56</sup>. The attraction of THz imaging is largely due to the availability of phase-sensitive spectroscopic images, which holds the potential for material identification or ‘functional imaging’.

THz systems are ideal for imaging dry dielectric substances including paper, plastics and ceramics. These materials are relatively non-absorbing in this frequency range, yet different materials may be easily discriminated on the basis of their refractive index, which is extracted from the THz phase information. Many such materials are opaque at optical frequencies, and provide very low contrast for X-rays. THz imaging systems may therefore find important niche applications in security screening and manufacturing quality control. An important goal in this context is the development of three-dimensional (3D) tomographic T-ray imaging systems<sup>57</sup>. Figure 5 illustrates a reconstructed cross section and 3D-rendered image of two plastic cylinders with differing refractive index. The system is based on the same principles as X-ray computed tomography, but provides a wealth of information about the material’s frequency-dependent optical properties through broadband, phase-sensitive THz detection<sup>58</sup>.

Interest in using THz imaging to study cellular structure is also increasing. A fundamental limitation in this context is the resolution of current systems. The Rayleigh criterion limits the far-field resolution of an imaging system to the order of the wavelength (0.3 mm at 1 THz). For this reason, researchers are relying on imaging in the near-field to achieve improved spatial resolution. Using near-field techniques, similar to those used in near-field optical microscopy, resolutions of 7  $\mu\text{m}$  have been demonstrated using radiation with a centre wavelength of 600  $\mu\text{m}$  (ref. 59). An alternative method to improve the resolution is to use higher-frequency THz pulses. Figure 6 shows a THz image of a membrane of onion cells. The resolution of approximately 50  $\mu\text{m}$  is achieved by using very broadband THz pulses extending into the mid-infrared. The contrast in the image is attributed primarily to differences in the water content of the cells and the intercellular regions<sup>60</sup>.

#### BIOMATERIAL THz APPLICATIONS

THz systems have broad applicability in a biomedical context. Active fields of research range from cancer detection<sup>61</sup> to genetic analysis. Biomedical applications of THz spectroscopy are facilitated by the fact that the collective vibrational modes of many proteins and DNA molecules are predicted to occur in the THz range. THz spectroscopy has also been heralded for its potential ability to infer information on a biomolecule’s conformational state. The complex refractive index of pressed pellets consisting of DNA and other biomolecules has been determined and shows absorption consistent with a large density of low-frequency infrared-active modes<sup>62,63</sup>.

DNA analysers are used to identify polynucleotide base sequences for a variety of genetic applications. Production of gene chips is an increasingly popular technique where unknown DNA molecules are bound to fluorescently labelled polynucleotides with known base sequences. Fluorescent labelling can affect diagnostic accuracy and increases the cost and preparation time of gene chips. As a result, several ‘label-free’ methods are being researched. THz imaging appears to have promise in this context. THz spectroscopy has shown the capability of differentiating

between single- and double-stranded DNA owing to associated changes in refractive index<sup>64</sup>. Recently the same group has demonstrated a THz sensing system capable of detecting DNA mutations of a single base pair with femtomole sensitivity<sup>2</sup>.

A further biomedical application of THz systems is the T-ray biosensor<sup>65</sup>. A simple biosensor has been demonstrated for detecting the glycoprotein avidin after binding with vitamin H (biotin). A film of biotin is deposited on a solid substrate (Fig. 7a), and half of the biosensor slide is exposed to the environment or solution of interest. Avidin has a very strong affinity for biotin and binds to any biotin-containing molecules. The modified far-infrared optical properties of the bound biotin film can then be detected using the technique of differential THz-TDS<sup>66</sup>. The slide is mounted on a galvanometric shaker and the THz beam is alternately focused through the avidin and control portion of the slide (Fig. 7b). A comparison of the signal measured using a slide treated with 0.3 ng cm<sup>-2</sup> avidin solution and a plain biotin slide revealed a detectable difference (Fig. 7c). This detectable limit is significantly enhanced by chemically binding the avidin molecules to agarose beads to provide increased contrast of refractive index<sup>67</sup>. Such techniques may find broad applications in trace gas sensing and proteomics.

## OUTLOOK

THz spectroscopy systems have undergone dramatic changes over the past decade. Improved source and detector performance continue to expand application areas and facilitate the transition of THz systems from the laboratory to commercial industry. Biomedical imaging and genetic diagnostics are two of the most obvious potential applications of this technology, but equally promising is the ability to investigate material characteristics, probe distant galaxies and study quantum interactions. THz radiation has further potential for revolutionary new uses, such as in the manipulation of bound atoms, which holds potential for future quantum computers<sup>68</sup>. Several key research areas promise significant continuing advances in THz technology. Central among these are current efforts towards higher-power THz sources—which will give rise to non-linear THz spectroscopy, with the potential to extract additional material characteristics—higher-sensitivity receivers and improved understanding of the interaction between THz radiation and materials such as quantum structures and biomaterials.

## References

- Kohler, R. *et al.* Terahertz semiconductor-heterostructure laser. *Nature* **417**, 156–159 (2002).
- Nagel, M., Haring Bolivar, P., Brucherseifer, M. & Kurz, H. Integrated THz technology for label-free genetic diagnostics. *Appl. Phys. Lett.* **80**, 154–156 (2002).
- Huber, R. *et al.* How many-particle interactions develop after ultrafast excitation of an electron-hole plasma. *Nature* **414**, 286–289 (2001).
- Auston, D. H., Cheung, K. P., Valdmanis, J. A. & Kleinman, D. A. Cherenkov radiation from femtosecond optical pulses in electro-optic media. *Phys. Rev. Lett.* **53**, 1555–1558 (1984).
- Fattinger, Ch. & Grischkowsky, D. Point source terahertz optics. *Appl. Phys. Lett.* **53**, 1480–1482 (1988).
- Ferguson, B. & Abbott, D. De-noising techniques for terahertz responses of biological samples. *Microelectron. J.* **32**, 943–953 (2001).
- Hashimshony, D., Ziegler, A. & Papadopoulos, D. Conversion of electrostatic to

- electromagnetic waves by superluminous ionization fronts. *Phys. Rev. Lett.* **86**, 2806–2809 (2001).
- van der Weide, D. W., Murakowski, J. & Keilmann, F. Gas-absorption spectroscopy with electronic terahertz techniques. *IEEE Trans. Microwave Theory Tech.* **48**, 740–743 (2000).
- Mourou, G. A., Stancampiano, C. V., Antonetti, A. & Orszag, A. Picosecond microwave pulses generated with a subpicosecond laser driven semiconductor switch. *Appl. Phys. Lett.* **39**, 295–296 (1981).
- Gornik, E. & Kersting, R. in *Semiconductors and Semimetals* (ed. Tsien, K. T.) (Academic, San Diego, 2001).
- Leitenstorfer, A., Hunsche, S., Shah, J., Nuss, M. C. & Knox, W. H. Femtosecond charge transport in polar semiconductors. *Phys. Rev. Lett.* **82**, 5140–5142 (1999).
- Leitenstorfer, A., Hunsche, S., Shah, J., Nuss, M. C. & Knox, W. H. Femtosecond high-field transport in compound semiconductors. *Phys. Rev. B* **61**, 16642–16652 (1999).
- Darrow, J. T., Zhang, X.-C., Auston, D. H. & Morse, J. D. Saturation properties of large-aperture photoconductor antennas. *IEEE J. Quantum Electron.* **28**, 1607–1616 (1992).
- Zhao, G., Schouten, R. N., van der Valk, N., Wenckebach, W. T. & Planken, P. C. M. Design and performance of a THz emission and detection setup based on a semi-insulating GaAs emitter. *Rev. Sci. Instrum.* **73**, 1715–1719 (2002).
- Katzenellenbogen, N. & Grischkowsky, D. Efficient generation of 380 fs pulses of THz radiation by ultrafast laser pulse excitation of a biased metal-semiconductor interface. *Appl. Phys. Lett.* **58**, 222–224 (1991).
- Bass, M., Franken, P. A., Ward, J. E. & Weinreich, G. Optical rectification. *Phys. Rev. Lett.* **9**, 446–448 (1962).
- Yang, K. H., Richards, P. L. & Shen, Y. R. Generation of far-infrared radiation by picosecond light pulses in LiNbO<sub>3</sub>. *Appl. Phys. Lett.* **19**, 320–323 (1971).
- Zhang, X.-C., Jin, Y., Yang, K. & Schowalter, L. J. Resonant nonlinear susceptibility near the GaAs band gap. *Phys. Rev. Lett.* **69**, 2303–2306 (1992).
- Rice, A. *et al.* Terahertz optical rectification from <110> zinc-blende crystals. *Appl. Phys. Lett.* **64**, 1324–1326 (1994).
- Zhang, X.-C. *et al.* Terahertz optical rectification from a nonlinear organic crystal. *Appl. Phys. Lett.* **61**, 3080–3082 (1992).
- Bonvalet, A., Joffe, M., Martin, J.-L. & Migus, A. Generation of ultrabroadband femtosecond pulses in the mid-infrared by optical rectification of 15 fs light pulses at 100 MHz repetition rate. *Appl. Phys. Lett.* **67**, 2907–2909 (1995).
- Kaindl, R. A., Eickemeyer, F., Woerner, M. & Elsaesser, T. Broadband phase-matched difference frequency mixing of femtosecond pulses in GaSe: Experiment and theory. *Appl. Phys. Lett.* **75**, 1060–1062 (1999).
- Huber, R., Brodschelm, A., Tauser, F. & Leitenstorfer, A. Generation and fields-resolved detection of femtosecond electromagnetic pulses tunable up to 41 THz. *Appl. Phys. Lett.* **76**, 3191–3193 (2000).
- Wiltse, J. C. History of millimeter and submillimeter waves. *IEEE Trans. Microwave Theory Technol.* **32**, 1118–1127, (1984).
- Siegel, P. H. Terahertz technology. *IEEE Trans. Microwave Theory Technol.* **50**, 910–928 (2002).
- Maiwald, F. *et al.* in *IEEE Microwave Theory and Techniques Society International Symposium Digest* (ed. Sigmon, B.) Vol. 3 1637–1640 (IEEE, Piscataway, New Jersey, 2001).
- Ryzhii, V., Khmyrova, I. & Shur, M. S. Terahertz photomixing in quantum well structures using resonant excitation of plasma oscillations. *J. Appl. Phys.* **91**, 1875–1881 (2002).
- Williams, G. P. Far-IR/THz radiation from the Jefferson Laboratory, energy recovered linac, free electron laser. *Rev. Sci. Instrum.* **73**, 1461–1463 (2002).
- Morris, R. & Shen, Y. R. Theory of far-infrared generation by optical mixing. *Phys. Rev. A*, **15**, 1143–1156 (1977).
- Brown, E. R., McIntosh, K. A., Nichols, K. B. & Dennis, C. L. Photomixing up to 3.8 THz in low-temperature-grown GaAs. *Appl. Phys. Lett.* **66**, 285–287 (1995).
- Kawase, K., Sato, M., Taniuchi, T. & Ito, H. Coherent tunable THz-wave generation from LiNbO<sub>3</sub> with monolithic grating coupler. *Appl. Phys. Lett.* **68**, 2483–2485 (1996).
- Shikata, J., Kawase, K., Sato, M., Taniuchi, T. & Ito, H. Enhancement of THz-wave output from LiNbO<sub>3</sub> optical parametric oscillators by cryogenic cooling. *Opt. Lett.* **24**, 202–204 (1999).
- Kawase, K., Shikata, J., Imai, K. & Ito, H. Transform-limited, narrow-linewidth, terahertz-wave parametric generator. *Appl. Phys. Lett.* **78**, 2819–2821 (2001).
- Kadow, C., Jackson, A. W., Gossard, A. C., Matsura, S. & Blake, G. A. Self-assembled ErAs islands in GaAs for optical-heterodyne terahertz generation. *Appl. Phys. Lett.* **76**, 3510–3512 (2000).
- Komiyama, S. Far-infrared emission from population-inverted hot-carrier system in p-Ge. *Phys. Rev. Lett.* **48**, 271 (1982).
- Goussev, Yu. P. *et al.* Widely tunable continuous wave THz laser. *Appl. Phys. Lett.* **75**, 757–759 (1999).
- Faist, J. *et al.* Quantum cascade laser. *Science* **264**, 553–556 (1994).
- Komiyama, S., Astafiev, O., Antonov, V., Kutsuwa, T. & Hirai, H. A single-photon detector in the far-infrared range. *Nature* **403**, 405–407 (2000).
- Gaidis, M. C. *et al.* A 2.5 THz receiver front-end for spaceborne applications. *IEEE Trans. Microwave Theory Technol.* **48**, 733–739 (2000).

40. Dolan, G. J., Phillips, T. G. & Woody, D. P. Low noise 115 GHz mixing in superconductor oxide barrier tunnel junctions. *Appl. Phys. Lett.* **34**, 347–349 (1979).
41. Carlstrom, J. E. & Zmuidzinas, J. in *Reviews of Radio Science* (ed. Stone, W. R.) 1193–1995 (Oxford Univ. Press, Oxford, UK, 1996).
42. Knap, W. *et al.* Resonant detection of sub-terahertz radiation by plasma waves in the submicron field effect transistor. *Appl. Phys. Lett.* **80**, 3433–3435 (2002).
43. Valdmantis, J. A., Mourou, G. A. & Gabel, C. W. Subpicosecond electrical sampling. *IEEE J. of Quantum Electron.* **19**, 664–667 (1983).
44. Wu, Q. & Zhang, X.-C. Free-space electro-optic sampling of terahertz beams. *Appl. Phys. Lett.* **67**, 3523–3525 (1995).
45. Brodschelm, A., Tauser, F., Huber, R., Sohn, J. Y. & Leitenstorfer, A. in *Ultrafast Phenomena XII* (eds. Elsaesser, T., Mukhamel, S., Murnane, M. M. & Scherer, N. F.) (Springer, Berlin, 2000).
46. Kono, S., Tani, M., Gu P. & Sakai, K. Detection of up to 20 THz with a low-temperature-grown GaAs photoconductive antenna gated with 15 fs light pulses. *Appl. Phys. Lett.* **77**, 4104–4106 (2001).
47. Holland, W. S. *et al.* Submillimeter images of dusty debris around nearby stars. *Nature* **392**, 788–791 (1998).
48. van Exter, M., Fattinger, C. & Grischkowsky, D. Terahertz time-domain spectroscopy of water vapor. *Opt. Lett.* **14**, 1128–1130 (1989).
49. van Exter, M. & Grischkowsky, D. Characterization of an optoelectronic terahertz beam system. *IEEE Trans. Microwave Theory Tech.* **38**, 1684–1691 (1990).
50. Grischkowsky, D., Keiding, S., van Exter, M. & Fattinger, C. Far-infrared time-domain spectroscopy with terahertz beams of dielectrics and semiconductors. *J. Opt. Safety Am. B* **7**, 2006–2015 (1990).
51. Jiang, Z., Li, M. & Zhang, X.-C. Dielectric constant measurement of thin films by differential time-domain spectroscopy. *Appl. Phys. Lett.* **76**, 3221–3223 (2000).
52. Kaindl, R. A. *et al.* Far-infrared optical conductivity gap in superconducting MgB<sub>2</sub> films. *Phys. Rev. Lett.* **88**, 027003 (2002).
53. Hu, B. B. & Nuss, M. C. Imaging with terahertz waves. *Opt. Lett.* **20**, 1716–1718 (1995).
54. Mittleman, D. M., Jacobsen, R. H. & Nuss, M. C. T-ray imaging. *IEEE J. Sel. Top. Quantum Electron.* **2**, 689–692 (1996).
55. Löffler, T. *et al.* Terahertz dark-field imaging of biomedical tissue. *Optics Express* **9**, 616–621 (2001).
56. Cheville, R. A. & Grischkowsky, D. Far-infrared terahertz time-domain spectroscopy of flames. *Opt. Lett.* **20**, 1646–1648 (1995).
57. Ferguson, B., Wang, S., Gray, D., Abbott, D. & Zhang, X.-C. T-ray computed tomography. *Opt. Lett.* **27**, 1312–1314 (2002).
58. Ferguson, B., Wang, S., Gray, D., Abbott, D. & Zhang, X.-C. Towards functional 3D THz imaging. *Phys. Med. Biol.* (in the press).
59. Mitrofanov, O. *et al.* Collection-mode near-field imaging with 0.5-THz pulses. *IEEE J. Sel. Top. Quantum. Electron.* **7**, 600–607 (2001).
60. Han, P. Y., Cho, G. C. & Zhang, X.-C. Time-domain transillumination of biological tissues with terahertz pulses. *Opt. Lett.* **25**, 242–245 (2000).
61. Woodward, R. M. *et al.* in *OSA Trends in Optics and Photonics (TOPS)*, Vol 56, *Conference on Lasers and Electro-optics*. (OSA, Washington DC, 2001).
62. Markelz, A. G., Roitberg, A. & Heilweil, E. J. Pulsed terahertz spectroscopy of DNA, bovine serum albumin and collagen between 0.1 and 2.0 THz. *Chem. Phys. Lett.* **320**, 42–48 (2000).
63. Walther, M., Fischer, B., Schall, M., Helm H. & Uhd Jepsen, P. Far-infrared vibrational spectra of all-trans, 9-cis and 13-cis retinal measured by THz time-domain spectroscopy. *Chem. Phys. Lett.* **332**, 389–395 (2000).
64. Brucherseifer, M. *et al.* Label-free probing of the binding state of DNA by time-domain terahertz sensing. *Appl. Phys. Lett.* **77**, 4049–4051 (2000).
65. Mickan, S. P. *et al.* Label-free bioaffinity detection using Terahertz technology. *Phys. Med. Biol.* (in the press).
66. Mickan, S. P., Abbott, D., Munch, J. & Zhang, X.-C. Noise reduction in Terahertz thin film measurements using a double modulated differential technique. *Fluct. Noise Lett.* **2**, 13–28 (2002).
67. Menikh, A., MacColl, R., Mannella, C. A. & Zhang, X.-C. Terahertz biosensing technology: Frontiers and progress. *Chem. Phys. Chem.* (in the press).
68. Cole, B. E., Williams, J. B., King, B. T., Sherwin, M. S. & Stanley, C. R. Coherent manipulation of semiconductor quantum bits with terahertz radiation. *Nature* **410**, 60–65 (2001).

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