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REVIEW ARTICLE

Terahertz Technology : An Overview

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ABSTRACT

Terahertz technology is the novel techniques for the physical characterization of pharmaceutical drug materials and final solid dosage forms, utilizing spectral information in the far infrared region of the electromagnetic spectrum. There is a need for ever more effective security screening to detect an increasing variety of threats. Many techniques employing different parts of the electromagnetic spectrum from radio up to X- and gamma-ray are in use. Terahertz radiation, which lies between microwave and infrared, is the last part to be exploited for want, until the last few years, of suitable sources and detectors. Terahertz imaging and spectroscopy has been shown to have the potential to use very low levels of this non- ionising radiation.

Keywords: Terahertz, Security screening, Narrow Band sources, Bolometers.

INTRODUCTION

Within the electromagnetic spectrum (between DC and gamma rays) the last portion to be examined lies between millimeter waves and long-wave infrared. In terms of frequency, this region extends 3 decades, from roughly 300 GHz to about 300 THz. Other ranges may be referred to as “THz,” but they vary only in the specific upper and lower boundaries. The key point to remember is that this range lies between what is commonly known as the highest “microwave” frequencies and the longest wavelengths of “light waves” in the infrared region.(1)

Terahertz radiation (THz) is in a region of the electromagnetic spectrum between the Infrared and Microwave frequency ranges, which is as yet largely untapped in terms of its potential applications. However, as noted in a recent Foresight study, the appearance of relatively cheap, coherent (laser) sources and detectors for Terahertz radiation is now leading to the exploitation of this spectral region being investigated seriously.(2)

The key features of THz radiation are that it can penetrate a wide range of materials such as human tissue, clothing, paper, wood, plastic and ceramics and that being non-ionising (unlike X-rays), it is not expected to damage DNA. These properties open up a variety of future commercial opportunities of which security and medical imaging applications offer perhaps the greatest potential.(3)However, that at the present time, the majority of systems under evaluation for security screening at airports, railway stations and the like, appear to operate in the adjacent ‘Millimetre Wave’ region, despite in some cases being referred to as using Terahertz technology.(4) The first commercial Terahertz imaging and spectroscopic systems are now becoming available and in addition to medical and surveillance uses, applications are foreseen in drug discovery and non-destructive testing of foodstuffs, coatings and semi-conductor chips.

Terahertz technology

Over the past few years terahertz technology has become a new tool for the physical characterization of solid materials. Radiation in the far-infrared region of the electromagnetic spectrum, so-called terahertz radiation (60 GHz–4 THz = 2–130 cm−1) is used to study pharmaceutical materials. Both imaging and spectroscopic measurements have been developed. Using this technology it is possible to directly access and exploit structural information of condensed matter at unparalleled speed. The energies of terahertz radiation are lower than most internal vibrations of the molecules and the predominant mode of absorption of terahertz radiation is due to intermolecular vibrations. Using femto second lasers and specially-designed photoconductive semiconductor antenna switches, terahertz radiation can be generated and detected at room temperature using a time-gated coherent detection scheme. Pulses of laser light, with photon energy greater than the bandgap of the gallium arsenide (GaAs) semiconductor, generate electron-hole pairs in the substrate. These photo-injected charge carriers are subsequently accelerated through the substrate by a direct current electric field. [5][6]

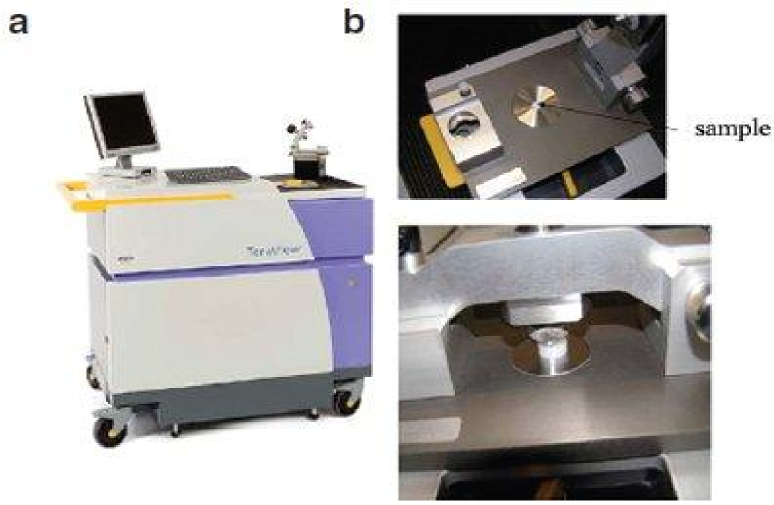

Figure 1: Terahertz Instrument

THz Research History

The last gap in the spectrum was bridged in 1923, when Ernest Nichols and J.D. Tear finally completed their efforts to observe radiation in the THz range. Their work was a systematic approach, both upwards in frequency from the microwave region and downward from the infrared region. Before this more-or-less official conclusion of the search, there were many significant contributions to THz range understanding. In 1900, in Germany, Rubens and Kurlbaum applied earlier work Rubens had done in collaboration with Nichols, resulting in accurate experimental data at longer wavelengths than had been previously observed. Max Planck wrote the equation that would become Planck’s Radiation Law on the same day that Rubens showed him those results. Other experimental work in the THz region also made significant contributions. Initially, optical techniques of gratings, interference, refraction, etc. were only partially successful at THz frequencies, and radiometers were not very sensitive. As a result, much work was done to analyze data indirectly at harmonics that fell into the infrared range where measurements could readily be made. [1]

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Basics

The electromagnetic range that is used is very vast. At low frequencies end we have radio waves up to millimeter waves, and at the other end we have optical waves down to the far infrared. Technologies have been developed for both ends of the spectrum which we use in everyday applications. But the terahertz region:

0.1 − 10 THz 1 THz = 1012 Hz

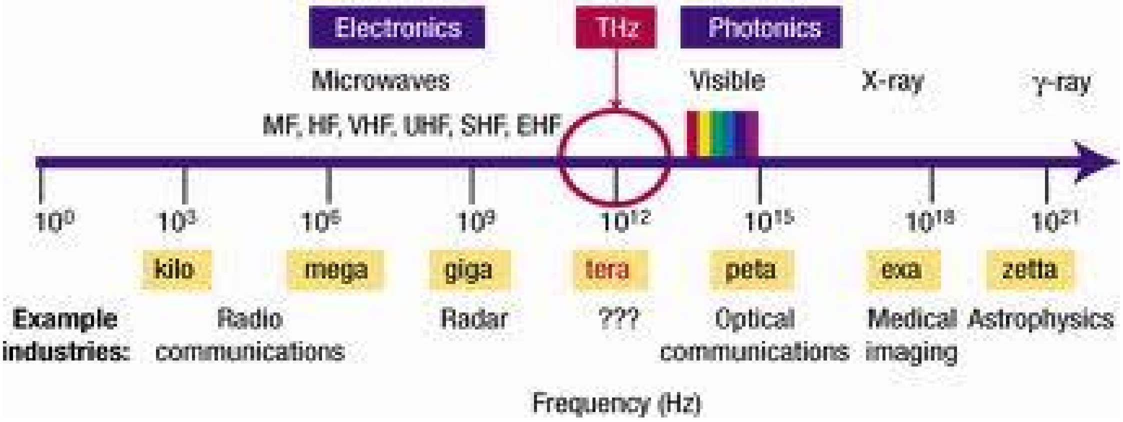

Figure 2: the Terahertz Gap

It is possible to produce effectively radiation in the low frequency region (microwaves) with oscillating circuits based on high-speed transistors and at high frequencies (visible spectrum) with semiconductor lasers. But transistors and other electric devices based on electric transport have in principle a limit at about 300 GHz, but are practically limited to about 50 GHz, because devices above this are extremely inefficient, and the frequency of semiconductor lasers can only be extended down to about 30 THz. Thus there is a region in between where both technologies do not meet. This region is often referred to as the terahertz gap. [7]

Terahertz System

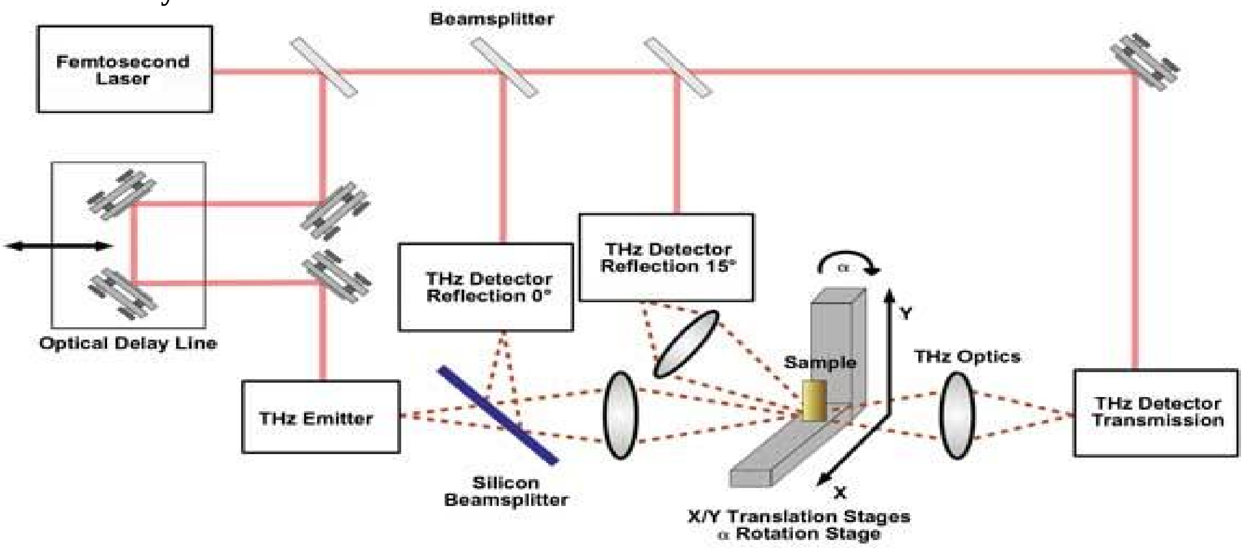

Figure: 3 terahertz system

A. Sources for THz radiation

Due to the lack of high power, portable, room temperature THz sources is the most significant limitation of THz systems. For this reason this is a very lively research field. Some very promising new approaches have the potential to bring terahertz technology a step further to everyday applications. But these sources are still not fully developed technologies.

1. **Normal THz sources :**

THz radiation is naturally emitted by all bodies. The blackbody radiation in this spectral range, below the far infrared, is comparatively weak - lower than 1μW per cm^{-3}. Sources like light bulbs in the visible spectrum are therefore unsuitable.

2. **Broadband sources :**

Broadband pulsed THz sources based on the excitation of different materials with ultra short laser pulses. These are photo carrier acceleration in photo conducting antennas, second order non-linear effects in electro optic crystals, plasma oscillations, and electronic non linear transmission lines. Unfortunately most of the different technologies have very low conversion efficiencies (nano to micro watts compared to about 1 W power from the optical source).

According to these photoconductive emitters are capable of relatively large average THz powers of 40 μW and bandwidths as high as 4 THz. This source operates with comparatively low power, but the beam is stable and coherent with well known temporal characteristics. Hence it is used for spectroscopy with high spectral resolution and excellent signal-to noise ratio and for imaging technologies.

3. **Narrowband sources :**

The techniques under development range from up conversion of radio frequency sources to different kinds of lasers, including gas lasers, free electron lasers, and in particular quantum cascade lasers. One technique to generate (low power) continuous wave THz radiation is through up conversion of lower frequency microwave oscillators. Frequencies up to 2.7 THz have been demonstrated. Another common source are gas lasers. The gases used are mainly methanol and hydrogen cyanide. In this method a Co^2 laser pumps a low-pressure gas cavity with one of the gases mentioned, which lasers at the gas molecules emission lines. These frequencies are not continuous tuneable and require large cavities and high (kilowatts) power supplies with only output power of the magnitude of milli Watts. These lasers are tuneable through the applied magnetic field or external stress. But they have many inherent limitations such as low efficiency, low output power, and the need for cryogenic cooling.

Another approach to build semiconductor lasers in the terahertz region is based on the newer technique of a Quantum Cascade Laser. These lasers were first demonstrated in 1994. A Quantum Cascade Laser consists of periodic layers of two semiconductor materials, which form a series of coupled quantum wells and barriers with a repeating structure. [(8)(9)]

B. Terahertz Detectors

The detection of THz radiation necessitates very sensitive methods, as sources come with low output power and the thermal background radiation is comparatively high. For broadband detection direct detectors are based on thermal absorption commonly used. These systems require cooling to reduce the thermal background. Systems common used are helium cooled silicon, germanium, and. Bolometers measure the incidented electromagnetic radiation through absorption and the resulting heating. The heating in turn is measured through the change in resistance. Extremely sensitive bolometers are based on the change of state of a superconductor such as niobium.

C. Terahertz Spectroscopy and Imaging system

It should be mentioned here that one can manipulate THz beams with mirrors and lenses as with light in the visible spectrum, but different materials have to be used. These are opaque for our eyes, but transparent for THz radiation. Two used materials are high resistivity silicon and high-density polyethylene. The former has no absorption or chromatic dispersion over the whole THz range, but has a high refraction index (3.42) and thus relatively large Fresnel losses. According to Fourier Transform Spectroscopy (FTS) is the most common technique for studying molecular resonances. With this technology one can characterise materials from THz to infrared frequencies. The sample is placed in an optical interferometer and illuminated with a broadband thermal source. Of interest is the path length difference of one of the interferometer arms. This technique is used in passive systems for monitoring thermal emission lines of molecules, particularly in astronomy applications. Another more recent technology is the THz Time Domain Spectroscopy (THz TDS). This method of measurement is also termed Terahertz Pulsed Imaging (TPI) and as the name suggests the dominant method of imaging. In this system the pulsed optical beam created by an ultrafast laser is splitted into a probe beam and a pump beam. The pump beam is incidented on the THz emitter (the THz source) to generate picosecond terahertz pulses. The terahertz radiation is collimated and then focused on the sample with parabolic mirrors. After transmission through the target the beam is collimated and refocused on the THz detector.These detectors can measure the electric field coherently. The optical probe beam is used to gate the detector and to measure the THz electric field instantaneously. At this the optical delay stage (computer controlled) is used to measure the transmitted terahertz pulse profile at a discrete number of time points to provide temporal information. [8][10]

Properties of THz radiation

THz radiation has some properties that open a wide range of applications, particularly for imaging. On the other have materials very interesting properties in this frequency range: Compared to microwaves, THz waves have more energy so they can penetrate deeper and make sharper images due to their shorter wavelength.

1. Water sensitivity

According to the minimum detectable water concentration is given by

$n \cdot x \_ 1016\text{cm}{-2}$

n is the density of water molecules and x is the length of the path traversed by the terahertz beam in the material.[11]

2. Safety / Medical implication

Implications on living tissue are not expected as T-Rays are non-ionising in contrast to xrays or ultraviolet (UV) light. Moreover, Terahertz signals are strongly absorbed by water, so that terahertz radiation cannot go through living tissue because of the high percentage of water in it.[12]

3. Theoretical prediction of water absorption

On one homepage of CoMIR the scientists say that preliminary measurements on tissue penetration have showed that predictions of attenuation based on water content alone have been incorrect. This group wants to develop a theoretical model for the absorption of terahertz radiation and compare the results with experimental measurements. So their work will show how safe the use of THz imaging is for living tissue. [13]

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Applications

We use x-ray scanners to examine luggage. Hospitals are equipped with ultrasound scanners and MRI (magneto resonance imaging) machines. In industry x-rays are used for package inspection and materials can be scanned for defects with microwaves or ultrasound. But although these technologies are very successful they all have shortcomings. In some cases these old techniques can be replaced by THz based methods, but there are also applications, which are unavailable with other frequencies, but possible with THz due to the characteristics of the materials as described before. Hence, many possible applications rely either on the extreme sensitivity of water or the ability to propagate through common packaging materials or both.

1. **Material Characterization**

For physics this new technology is very interesting because they can use it for characterization of materials like semiconductors and lightweight molecules. The radiation can be used to determine the carrier concentration and mobility of semiconductors, and in the superconductor research it can be used to determine the parameters of superconducting materials.(11)

2. **Quality Control**

THz imaging systems are ideal for imaging dry dielectric substances including paper, cardboard, thin wood, most plastics and ceramics, because these materials are relatively nonabsorbing in this frequency range. And additionally, these materials cannot be analysed with optical frequencies, because they are opaque for them or with x-rays, which have no absorption to provide contrast for imaging. Therefore spatially resolved transmission measurements can be used in the area of quality control of packaged goods.

3. **Study of Historical and Archaeological work**

Terahertz imaging methods work with extremely low powers, about 2 to 3 magnitudes of order lower than the blackbody radiation in this frequency range. The radiation is therefore non invasive to historical work, neither to paintings or paper in common nor to any kind of stone or metal. Thus this technique could be useful in history, archaeology etc.(14)

4. **Biology (Botany)**

This extreme sensitivity to water content is of great interest here as a method of measuring the water content of leaves on living plants. Currently there is no accepted non-destructive procedure for measuring the leaf water status of a transpiring plant. The cellular structure can be studied with THz as well. But a fundamental limit here is the resolution of current systems.

5. **Biomedical**

In the area of biomedical diagnostics we can make use of THz tomographie. Although there is a limited penetration depth of the radiation due to the strong water absorption, which excludes the use of THz radiation in most biomedical research areas, it can be used to examine tissue near the surface, in particular skin and teeth. On the other hand, the sensisensitive to water enables the investigation of tissue hydration. This opens a range of applications including analysis of burn depth and severity, and detection of skin cancer and caries. A reliable non-invasive probe of burn depth would be of great value to physicians, who currently have no such technology.

6. **Security checks (Airport)**

At airports or other security critical places dangerous non-metallic substances like ceramic knifes or plastic explosives now can be detected with terahertz beams. This is possible of the water content). The British company Qinetiq has tested such a system on airports already.(15)

7. **Molecular Structure**

The sensitivity and specificity of Terahertz spectroscopy to both intermolecular and intramolecular vibrations in different chemical species enable investigation of the crystalline

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state of drugs e.g. polymorphism. The use of pulsed terahertz imaging in proteomics and drug discovery determines protein 3D structure, folding and characterization. Terahertz spectroscopy provides rapid identification of the different crystalline forms of drug molecules – the polymorphs – which can display different solubilities, stabilities and bioavailability and therefore are an important factor in the therapeutic efficacy of a drug. Detecting and identifying the different polymorphs and understanding the mechanism and dynamics of polymorphic inter-conversion, is an important milestone in selecting the optimum form for further development and manufacture. Not only is it possible to detect the differences between pure specimens of the polymorphs but terahertz spectroscopy can distinguish between specific polymorphic forms in the tablet formulation. Terahertz spectroscopy can differentiate between different hydrate forms. Lactose, one of the most commonly used excipients in the pharmaceutical industry, forms at least three different hydrates: the most widely used α-monohydrate, the α-anhydrate and a β-anhydrate form. These three hydrate forms exhibit terahertz spectra that can be used for both quantitative and qualitative analysis.

8. Time resolved THz spectroscopy of protein folding

Proteins fold, catalyze reactions, and transduce signals via binding to other biomolecules. These processes are driven by motions with characteristic time scales ranging from femtoseconds (fs) to milliseconds (ms). The characteristic modes from which such motions collectively emerge often cause large amplitude deformations of all or part of the protein. Temperature tuning reveals when certain modes are frozen out, while the Terahertz spectroscopy can cover fast relaxation kinetics on fs time scale during which a protein rearranges its overall structure.

9. Pharmaceutical Industry: Tablet integrity and performance

Terahertz imaging gives an unparallel certainty about the integrity of tablet coatings and the matrix performance of tablet cores. Terahertz image can be optimized for performing 3D analysis on tablets. It can enable customers to determine coating integrity and thickness, detect and identify localized chemical/physical structure such as cracks or chemical agglomeration within a core and to interrogate embedded layers (such as an interface between two layers) for delamination and integrity. Terahertz measurements may well become the primary method for the nondestructive determination of coating thickness, requiring little or no calibration for most coatings and substrates. It can reveal the thickness, uniformity, distribution and coverage of simple and complex coatings. Terahertz image can also detect embedded layers and localized chemical/physical structural features in the cores of intact tablets to confirm 3D morphology and blend uniformity.

10. Terahertz in Dermatology

The cosmetic appearance of skin is directly linked to the state of its outermost layer, the stratum corneum. The water-content of the stratum corneum influences its permeability and elasticity. Most skin-care products such as moisturizers act to increase the retained water content of this layer of the skin to enhance its appearance. Quantitative characterization of the hydration-level of the stratum corneum is thus of crucial importance to the cosmetics industry in order to characterize and compare the effectiveness of their products.

11. Screening

The ability of terahertz technology to "see" through many opaque things such as clothing, box, shoe, etc. has led to successful proof of principle experiments at standoff distances for potential applications in building security, airports and defense. ARP has demonstrated direct imaging of hidden objects and set out to build the world's first practical direct terahertz imaging system, based on a hand held CCD camera that operates much like a regular video camera, but capable of detecting metallic and non metallic weapons and certain explosives. The Company will support defense and government agencies, as well as commercial partners, who wish to further explore this technology.

12. Tablet coating analysis

Analysis of tablet coatings is one of the major fields where terahertz technology is being applied to the pharmaceutical sciences. So far, the analysis of coating thickness and integrity has relied predominantly on indirect observations. Coating thickness is typically estimated from the weight gain of the coated tablets compared with the uncoated tablet cores. Even though these techniques revealed much additional information about the quality and integrity of coatings, the images were almost always confined to information reflected from the outside surface of the tablet. A different approach to characterize film coating defects at the interface between tablet coat and core was presented by means of confocal laser scanning microscopy. For sugar-coated products no such approach has been developed. To test the coating integrity, it is common practice to perform a dissolution study on part of the production batch. For analysis of the uniformity of a dosage form, buried structures within a dosage form, or multiple coating layers, destructive measurements have to be carried out. The tablets have to be cut layer by layer so that spectroscopic images can be acquired from each layer. This process is time-consuming and it is extremely difficult, if not impossible, to analyse such thin structures.[17]

13. 2D and 3D non-destructive chemical imaging

Combining the technology of TPI for tablet coating analysis and TPS for the analysis of the crystalline properties, and taking them one step further, non-destructive chemical recognition in a three-dimensional object has been performed in a proof-of-principle experiment. Spectral data were presented for a three-dimensional dataset with two axes describing the horizontal and vertical spatial dimensions, and the z-axis representing the depth information as signal time delay. A four-dimensional dataset was then generated by a time-partitioned Fourier transformation. This allowed the analysis of a pellet containing buried structures of different chemical composition. Different chemicals could be identified by their spectral signature in the 3D matrix of the sample. However promising these first results were, the work has to be considered as the first successful attempt to overcome the multitudinous challenges associated with the data acquisition and processing that need to be mastered to make 3D terahertz spectral imaging routinely applicable. Further work describes 2D chemical mapping of lactose amonohydrate, acetylsalicylic acid, sucrose and tartaric acid compressed pellets Terahertz 2D, and especially 3D chemical imaging, would enable the development of a number of exciting applications to further understand and improve pharmaceutical formulations.[18][19]

Layered tablets are increasingly being developed as products to alter the release kinetics of a drug or to combine incompatible drugs or excipients into one system. The recent advances in production technology not only allow these formulations to be produced but also create a demand for new technologies to analyse and understand them. The development of the 3D terahertz chemical imaging is still in its infancy and needs much further development. This technique potentially has a huge advantage over NIR imaging, as spectral data from within the sample can be acquired without destroying the sample. It would allow the analysis of the distribution of an API within its matrix of excipients before dissolution testing. Another interesting application could be the study of the rate and spatial distribution of drug decomposition processes during stability testing in-situ by quantitative chemometric models.[20]

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14. Other Applications

There are other applications of terahertz spectrometry and imaging. A few important ones are listed below:

- Food industry process control (e.g., moisture detection).
- Scientific: earth remote sensing, Environmental sensing (pollution detection), Plasma diagnostics.
- Seeing through sand storms, active and passive imaging through dust, smoke, fog etc; all weather active and passive seekers; secure communications; spectrographic sensing of explosives, gases and biologicals.
- High rate and secure data transfer, flame analysis (rocket or jet engine burn optimization).
- Homeland Security - concealed weapon identification, detection of suicide bombers, biological threat detection.
- Detection of voids in the space shuttle foam and in other structural materials.
- Passenger screening, hidden weapons detection, contraband detection.[16]

CONCLUSION

As sensors and sources become more available, more complex circuits and eventually complete instruments will follow. We have not even scratched the surface in this area and many more pages would be needed to do justice to the component developments that have taken place already at terahertz frequencies. On the instrument side, we are just beginning to see emerging systems. A terahertz network analyzer is commercially available, near-field antenna measurements have been performed at 640 GHz,12 a recently demonstrated millimeter-wave near field microscope technique promises micrometer resolution terahertz imaging once sources have been developed, the T-ray system is now being employed on a wide variety of samples from the electronics industry to medical diagnostics and will likely be the medium for introducing the public to terahertz wavelengths for the first time. As laser systems advance so that the pulsed and higher power bench-top models are replaced by solid-state semiconductor devices, there will be dramatic reductions in the instrument envelopes, as well as tremendous cost savings. All of these exciting applications and countless undiscovered ones remain in wait while terahertz technology enters adulthood it has been a long time coming and there is still much work to be done.[21][22]

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