

TeraView

in the pharmaceutical industry

Cutting edge applications span the pharmaceutical industry – from drug discovery through to manufacturing



- ▼ Early identification of polymorphism, crystallinity and amorphous materials in the research & development cycle
- ▼ Earlier selection of optimum, stable polymorphic forms of the API for development
- ▼ Non-destructive imaging of simple and complex tablet coatings for integrity checking and quality assurance during manufacture
- ▼ Detection of internal chemical and physical characteristics of dosage forms
- ▼ At-line QA sampling now, and in-line probing in development

TeraView is the first company to develop technologies which commercially exploit terahertz, the last unexplored region of the electromagnetic spectrum. Our patented terahertz technology creates spectroscopic information and 3D image maps with unique spectroscopic signatures not found at other wavelengths. It resolves many of the questions left unanswered by complementary techniques, such as optical imaging, Raman and infrared. Terahertz technology also produces faster results than X-ray and enables non-destructive, internal, chemical analysis of tablets, capsules and other dosage forms.

Born out of the Cavendish Laboratory – the world famous Department of Physics at the University of Cambridge – TeraView has nearly two decades of experience with terahertz technology and its application to solve customer problems.

Some 44 patented technologies underpin the innovation of Terahertz Pulsed Imaging (TPI™) embedded in our TeraView TPI Tablet Imager for 3D imaging and in the TeraView Spectra 1000 for spectroscopy.

Business context

At the discovery and product development stage, earlier identification of polymorphic variants enables resources to be directed to stable candidates and so speed the development process. During manufacture, the speed of results achieved by TeraView products supports at-line QA sampling, and is compatible with in-line probing. No other technology is able to provide such timely information and 3D images, while removing uncertainty about the effects of polymorphism both during development and manufacture.

As a result savings arise from faster time to market; volume production of consistent, high quality, stable products, and reduced waste.

TeraView's TPI technologies are fundamentally suited to the testing of complex tablet and coating forms. Their application facilitates improved process control and production consistency across plants and geographies. The technologies are particularly applicable to the FDA's Process Analytical Technologies (PAT) initiative. Moreover, TPI potentially provides a powerful platform for counterfeit detection.

TeraView applications across the drug development process



TeraView Spectra 1000

terahertz pulse spectroscopy of polymorphs

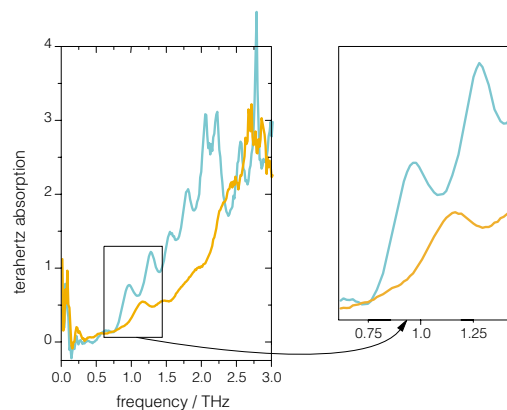


- ▼ Polymorph detection and identification
- ▼ Drug crystallinity and amorphous material detection
- ▼ Rapid sampling

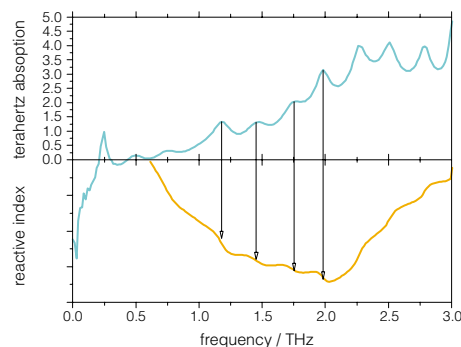
The TeraView Spectra 1000 provides rapid identification of the different crystalline forms of drug molecules

– 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 interconversion between them, is an important milestone in selecting the optimum form for further development and manufacture. The degree of crystallinity and amorphous content can also be monitored, and all these investigations can be carried out in the presence of excipients.

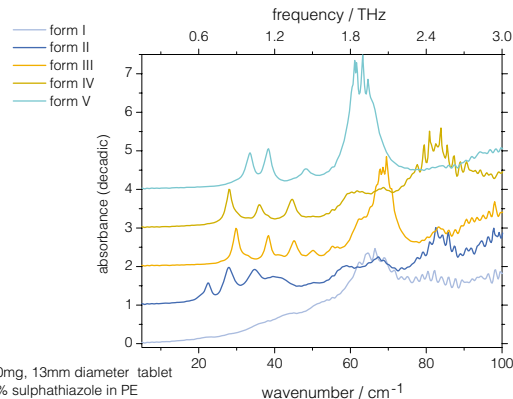
The TeraView Spectra 1000 detects polymorphs that cannot be identified with conventional methods. The ability to record spectra of a substance in a fraction of a second makes it compatible with high throughput screening approaches. TeraView is exploring the potential for rapid screening of pharmaceutical materials with the development of high throughput versions of the spectrometer.



Ranitidine hydrochloride polymorphs form I and form II

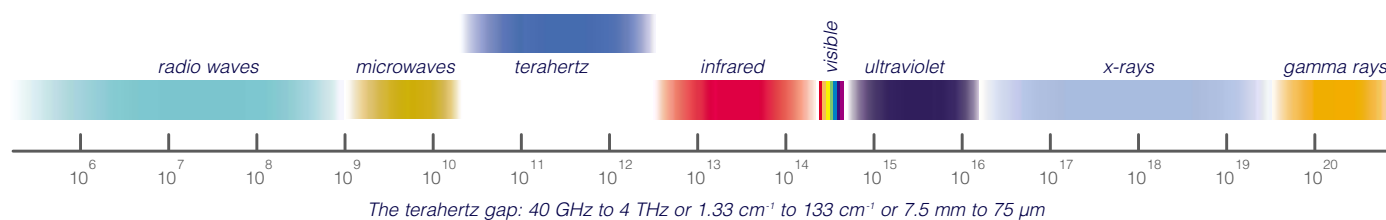


Ranitidine hydrochloride absorption spectrum and refractive index spectrum



Sulphathiazole polymorphs forms I to V

Terahertz and the spectral fingerprint



The terahertz gap: 40 GHz to 4 THz or 1.33 cm^{-1} to 133 cm^{-1} or 7.5 mm to 75 μm

The 'terahertz gap' – where until recently bright sources of light and sensitive means of detection did not exist – encompasses frequencies invisible to the naked eye in the electromagnetic spectrum, lying between microwave and infrared. TeraView's TPI core technology harnesses terahertz, which is intrinsically

safe, non-invasive and non-destructive, to create a powerful spectroscopic imaging technique for characterising molecular structures. TPI enables 3D imaging of structures and materials, and the measurement of the unique spectral fingerprints of different chemical and physical forms.

TeraView TPI Tablet Imager

3D image mapping of tablet coatings and content



TeraView's TPI Tablet Imager allows customers to image coating integrity and thickness as well as map the distribution of APIs or structural features introduced into the tablet and coatings as part of more advanced dosage forms. Imaging the distribution of pharmaceutical materials as well as other parameters such as granularity throughout

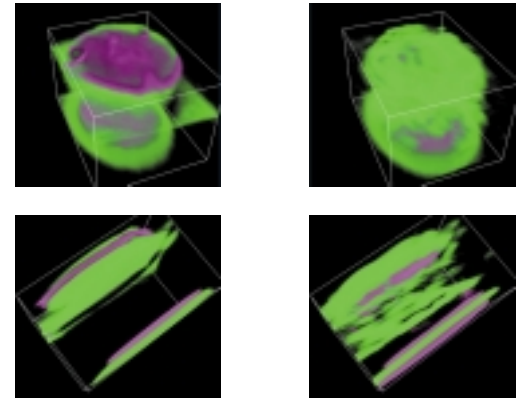
the tablet is also possible. The availability of rugged laser and fibre-fed technology, and the ability of the technique to rapidly image complete tablets, enables at-line and on-line applications to improve both quality assurance and control in manufacture.

The TeraView TPI Tablet Imager:

- ▼ provides 3D maps of thickness and integrity of both simple and complex coatings in controlled and sustained release products
- ▼ provides the 3D distribution of ingredients (API and excipients) in a tablet which affects dissolution and bioavailability
- ▼ ensures that the correct amount of API is used to minimise cost and ensure that safety (toxicity) standards are addressed
- ▼ confirms the stability of products by demonstrating that the 3D morphology is invariant
- ▼ enables counterfeit detection based on terahertz images of products which are characteristic of the production process used

Eight out of the ten most commonly prescribed drugs in the United States in 2001 are known to exhibit polymorphism or hydrate formation.

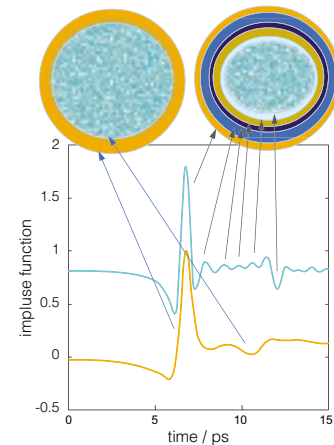
3D Tablet imaging



Model tablet without active ingredients

Model tablet with active ingredients

Identification of tablet coating structure



Comparison between different tablet constructions

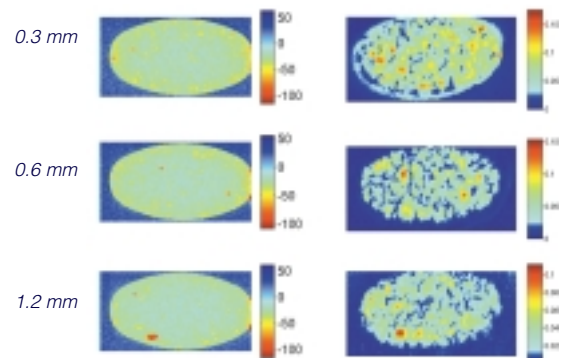
'Good' vs 'Poor' tablet coatings



'Good' – uniform outer coating thickness

'Poor' – poor uniformity of outer coating with holes

Comparison with X-Ray CT



X Ray images at different depths

TPI images at different depths

TeraView

Realising potential

TeraView Limited, based in Cambridge England, was spun-out of Toshiba Research Europe in April 2001 to exploit the intellectual property and expertise developed in sourcing and detecting terahertz (THz= 10^{12} Hz) radiation, using innovative semiconductor technologies. Leading proponents of the technology sit on our Advisory Board and TeraView maintains close links with the Cavendish Laboratory at the University of Cambridge, where modern terahertz technology was pioneered.

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Ref no. TVOVP-001

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