INFORME ESPECÍFICO DE APLICABILIDAD DE LA CAPACIDAD TECNOLÓGICA DIFERENCIAL ASTROFÍSICA EN LA OBTENCIÓN DE IMÁGENES BIOMÉDICAS CON RADIACIÓN TERAHERTZ

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SPECIFIC REPORT ON THE APPLICABILITY OF THE ASTROPHYSICAL DIFFERENTIAL TECHNOLOGICAL CAPACITY IN OBTAINING BIOMEDICAL IMAGES WITH TERAHERTZ RADIATION

Entregable Actividad 2.1.3

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1 Introduction: electromagnetic spectrum and terahertz radiation

The electromagnetic (EM) spectrum covers a huge range of frequencies or wavelengths as shown in Fig. 1. It is commonly divided into smaller sections, such as radio waves, microwaves, terahertz, infrared, visible light, ultraviolet, X-rays and gamma rays in terms of increasing frequency or decreasing wavelength. The distribution of the spectrum is shown in Fig. 1, with special focus on the terahertz band and its properties.

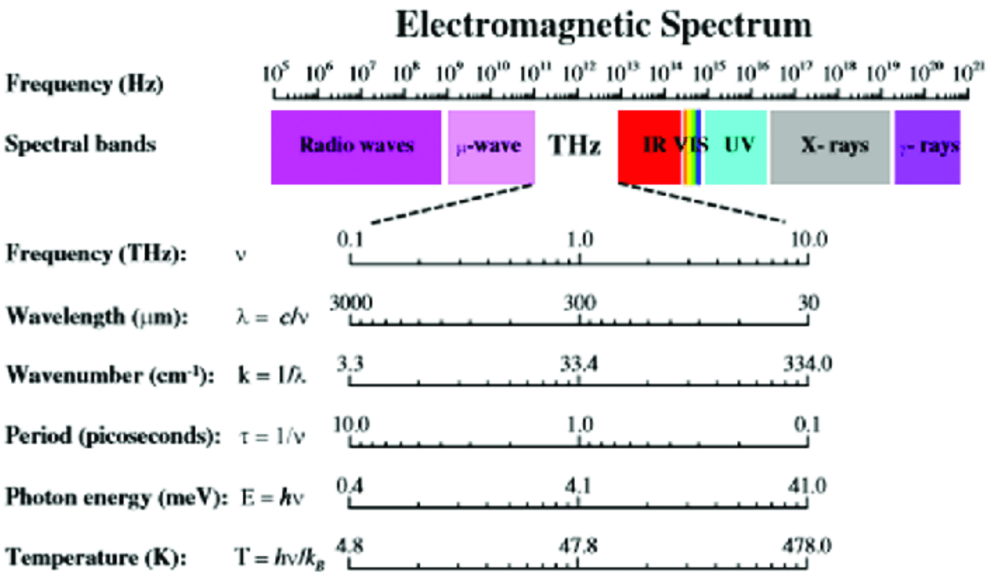

Fig. 1. Terahertz radiation band of the electromagnetic spectrum [1].

The terahertz (THz) radiation corresponds to the electromagnetic radiation covering the frequency range from 0.1 to 10 THz (tera = 10^{12}), or in wavelengths from 3 mm to 0.03 mm [2]. This radiation is also known as submillimeter radiation, terahertz waves, tremendously high frequency (THF), T-rays, T-waves, T-light or T-lux.

Terahertz radiation occupies a middle ground between microwaves and infrared light waves known as the "terahertz gap", where technology for its generation and manipulation is in its infancy. The generation and modulation of electromagnetic waves in this frequency range ceases to be possible by the conventional electronic devices used to generate radio waves and microwaves, requiring the development of new devices and techniques.

Terahertz radiation is in between infrared radiation and microwave radiation in the electromagnetic spectrum, sharing properties with both of them. Terahertz radiation is non-ionizing and, like microwaves, can penetrate a wide variety of non-conducting materials, such as clothing, paper, cardboard, wood, masonry, plastic or ceramics, but with lower penetration depth than that of microwave radiation. Moreover, terahertz radiation has limited penetration through fog and clouds and cannot penetrate liquid water or metal, like infrared radiation [3].

2 Terahertz radiation for medicine

Terahertz radiation provides outstanding features for biomedical purposes, since it is a non-ionizing radiation due to the low photon energy, the high sensitivity to water molecules and the capability of performing spectroscopic analysis [4]. This fact makes that THz radiation presents a significant advantage over X-ray technique due to it does not ionize molecules [5]. In addition, THz radiation is a remarkable source for medical studies, exhibiting high sensitivity in measurements targeting changes in biomolecules, cells or tissues, since this energy spectrum covers the characteristic energies of biomolecular collective motions [5].

However, the penetration depth into tissues is limited by the high sensitivity to water molecules, which is more important when specimens with high water content are considered. Thus, THz radiation can penetrate only a few hundred micrometers into human tissues since it is highly attenuated by water molecules [5]. On the other hand, this drawback is being overcome with different techniques, such as paraffin embedding, freezing and the use of enhancing gels [5-9].

Another significant disadvantage that requires to be beaten is the inhomogeneity of resonances in macromolecules. Different spectral peaks have appeared in different experiments with nucleobases, component of DNAs, but resonant features of the molecules have been hardly discovered [4].

Additionally, terahertz imaging could be applied for enhancing cancer diagnosis [10-12], contributing to the typical imaging procedures employed in those diseases. THz radiation is a promising technique over this area since most cancers start on the surface of soft tissues [5].

Furthermore, THz imaging is being employed in dermatological investigations, wound assessment and dental research [13], since the capability of reaching locations not easily accessible. However, the main requisite for any medical action with THz technology lies in the condition that the biological tissues are not damaged by the exposure to these EM fields [13].

Currently, THz biomedical imaging and research are mainly dedicated to diagnosis purposes by assessing the differences in water content in the tissues. Particularly, cancerous tissues may contain more interstitial water, which yield different THz absorption spectra and the differences in the structure of tissues can be also observed [13].

3 Biomedical applications of terahertz imaging

The early experiments focused on the measurement of THz radiation were commonly based on the characterization of black body radiation using bolometers [14]. Further investigation in the development of THz emitting sources, such as photoconductive emitter gated with an optical pulses, caused improvements in the detection of coherent THz radiation [14]. This achievement was the main issue to the development of THz time domain spectroscopy and imaging techniques pioneered in the mid-1990s.

Nowadays, the applications of THz technology for biomedical applications are mainly focused on [15]:

1. Capture the THz spectrum of biomolecule by THz spectroscopy, and the characteristic information of spectrum is used to recognize or classify biomolecules.

2. The applications of THz biological effects are still in research phase.

The THz spectroscopy refers to the measurement of THz radiation intensity as a function of wavelength and it is a fundamental exploratory tool in fields such as physics, chemistry and astronomy, allowing the investigation of the matter, in terms of its composition, physical structure and electronic structure. Therefore, important applications arise from biomedical spectroscopy in the areas of tissue analysis and medical imaging.

3.1 THz Spectroscopy

The THz radiation can be generated and detected in pulsed or continuous wave forms. Then, THz spectroscopy can be divided into different methods to measure the radiation: based on a time-domain analysis or based on Fourier transforms systems.

First, THz time-domain spectroscopy (TDS) is based on ultrafast lasers that excite with optical constants, in the form of the refractive index and absorption constant of the specimen, the material under analysis [5].

A TDS system obtains the amplitude and phase information of a THz wave passing through the sample [15]. A scheme of this system is shown in Fig. 2. THz–TDS can operate in transmission or reflection modes according to the employed measurement setting. Currently, THz–TDS has been widely employed in the detection of amino acids and polypeptides, DNA structure, protein, among others, as well as in the measurement of optical properties of biological tissues, chemical analysis or food quality control.

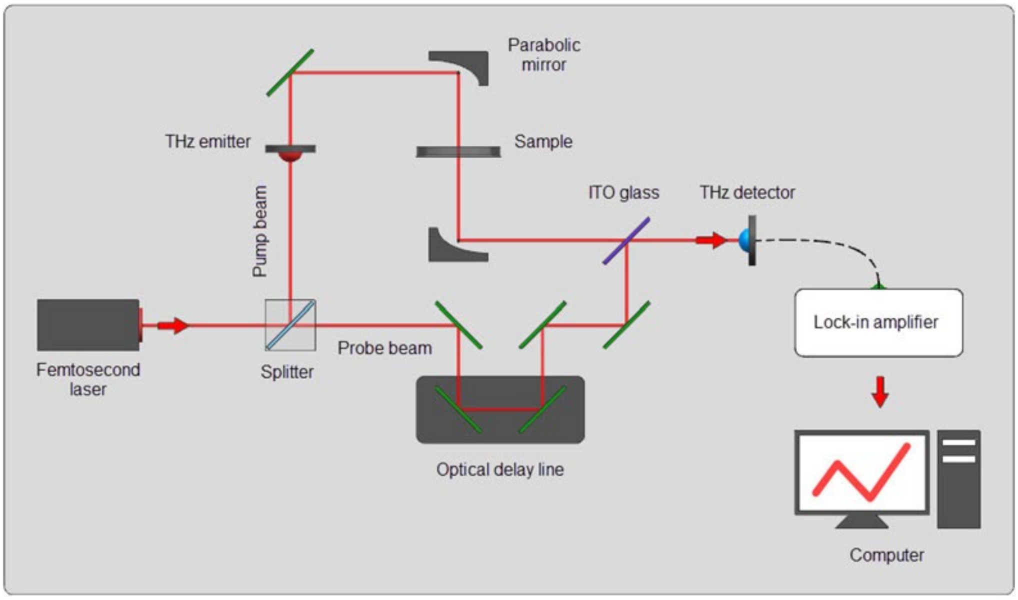

Fig. 2. Schematic diagram of THz–TDS system [15].

On the other hand, continuous wave (CW) sources and detectors offer an alternative without an ultrafast laser [5]. Several devices are available in this way as feasible source, such as high-speed transistors, resonant tunnelling diodes, quantum lasers or Schottky diodes among others. The single tone radiated from previously mentioned sources can be detected using bolometers, Schottky diode detectors or other optoelectronic detectors.

As an alternative spectroscopy technique, the Fourier transform infrared (FTIR) spectroscopy is also employed, particularly when the frequency range is above 3 THz [15]. This system employs a light emitting source, an interferometer, a sample cavity and its power controller, and a detector. A typical interferometric system is shown in Fig. 3.

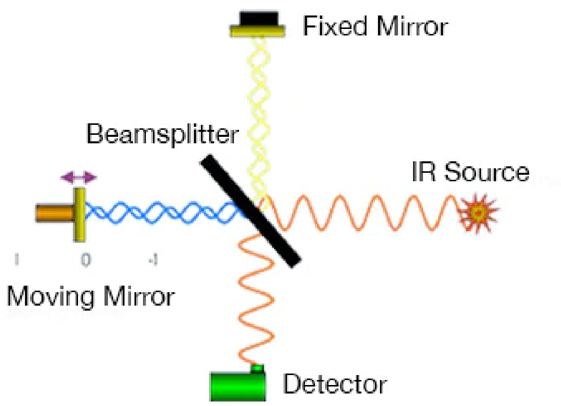

Fig. 3. Typical TFIR system based on an interferometer.

3.2 THz Imaging

THz imaging is based on the analysis and processing of the transmission and reflection spectrum information of the sample [15]. Imaging can be classified as pulsed THz imaging and continuous wave THz imaging regarding the form of the THz wave [15]. THz imaging shows the following advantages regarding traditional imaging technology:

1. It provides spectral information and spatial density distribution images of the samples under test.

2. Higher spatial resolution.

3. The sample is not destroyed.

Nevertheless, a critical issue when using THz imaging is the image acquisition speed [5]. Furthermore, although new faster detection equipment or advanced signal processing techniques are improving the scanning speed, large field of views are required for real-time imaging. Additionally, the high absorption of this radiation by liquid water significantly hinders the screening of internal body organs.

3.3 Frozen THz Imaging

As previously mentioned, the penetration depth of THz radiation in human tissues is a limiting factor. To overcome this fact, several researching activities have been performed focusing on freezing techniques into high water content tissues [5]. The lower absorption coefficient of frozen material than that of liquid water molecules support this activity [16-19]. Using this alternative, structural state of cells and chemical information of molecules in tissues can be observed, since the background effect induced by the water molecules is suppressed by freezing [5]. This technique is currently employed for tumour detection, lymphatic metastases and brain tissue samples for Alzheimer’s disease among others [5].

3.4 Penetration-enhancers THz Imaging

However, the above technique shows clinical limitations, since the freezing process might cause necrosis [5]. Therefore, external agents to enhance the penetration of the THZ radiation in the tissues have been employed into fresh samples. These agents should be biocompatible and easily absorbed into the tissues, as well as they should show a lower radiation absorption coefficient than water [5, 20-23]. Ethylene glycol has been studied as enhancer using reflectance spectroscopy [20]. Nevertheless, glycerol is an alcohol that provides a higher penetration than ethylene glycol when used as enhancer agent in the THz imaging technique [21, 23]. Finally, dimethyl sulfoxide (DMSO) has been also used as agent mitigating the attenuation in fresh tissues [22].

4 Terahertz imaging at IAC facilities

The IACTec engineering group is part of the Instituto de Astrofísica de Canarias (IAC) and it is deeply interested in applying the well-known astrophysical technology to biomedical imaging, by using the same kind of detectors.

The IAC has led for several years the characterization of visible and infrared detectors, as well as the development of acquisition systems and data processing for ground based and space instruments. Besides, the IAC has significant experience in the development of microwave systems for the same applications.

The THz radiation, also known as submillimetre radiation, is in the middle between microwaves and infrared light. This radiation is occasionally considered as part of these EM bands, particularly as part of the far infrared radiation, since it covers the frequency range above 200 GHz.

The IAC facilities are composed of several technical laboratories enabling the astrophysical imaging. Particularly, the IAC has a dedicated laboratory to characterize detectors, at room and cryogenic temperatures, in the following ranges of the EM spectrum:

· Visible light

· Short-wave near infrared (SWIR), wavelength < 1.6 micrometers

· Medium infrared (MWIR): wavelengths around 1/2.5/5 micrometers

· Far infrared (LWIR – thermal infrared): wavelengths between 8 and 14 micrometers

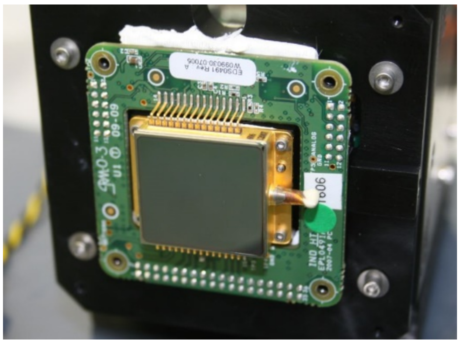

Fig. 4. Infrared microbolometer between 8 and 14 micrometers.

Fig. 5. Cryostat for characterizing cooled down detectors.

This facility could be adapted to the characterization of THz detectors in order to measure their performance, in combination with the Electronic Laboratory, in which microwaves experiments are being carried out up to frequencies of several hundreds of gigahertz.

Currently, the IAC is involved in a project operating at the THz band, particularly in the 145 and 220 GHz frequency bands [24-25]. The telescope is shown in Fig. 6.

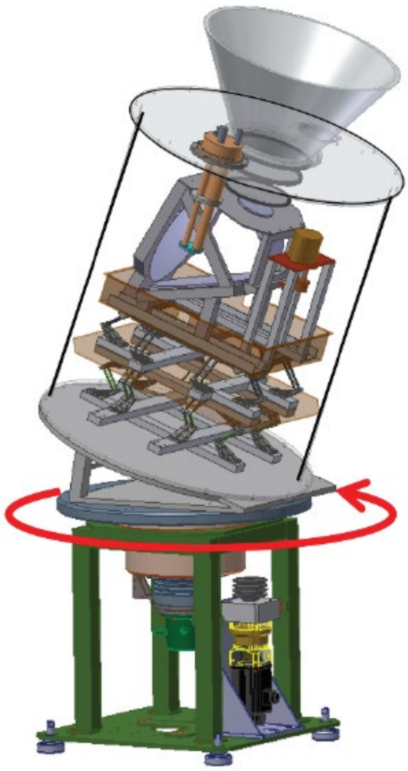

Fig. 6. Drawing of the telescope.

The technology developed for this telescope configures superconducting sensitive detectors, able to detect extremely low incoming powers. It operates at cryogenic temperature to reduce the noise power added by the instrument itself, and to enhance the conversion of the received signal. The development of this kind of detectors is a challenging issue, since the power to detect is tiny.

Finally, the IAC has an Optical Laboratory, composed of an ISO-8 clean room with controlled temperature and humidity conditions. This laboratory is equipped with optical instrumentation to characterize optical devices, such as lasers, filters, light sources and detectors.

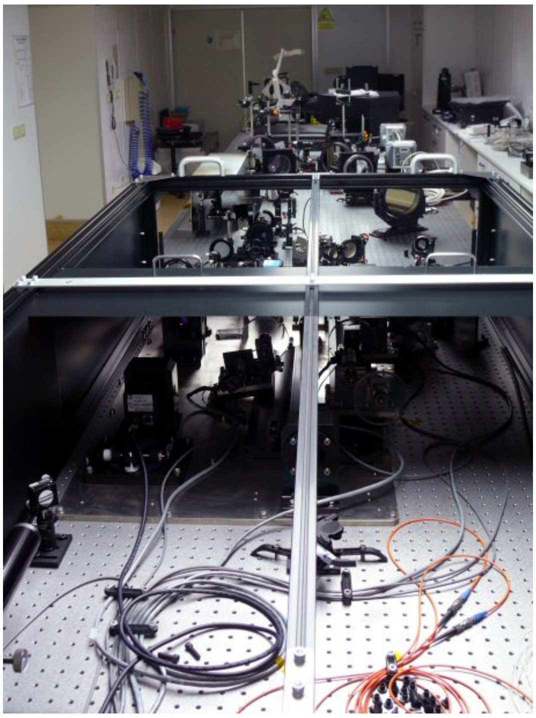

Fig. 7. Optical system inside the laboratory.

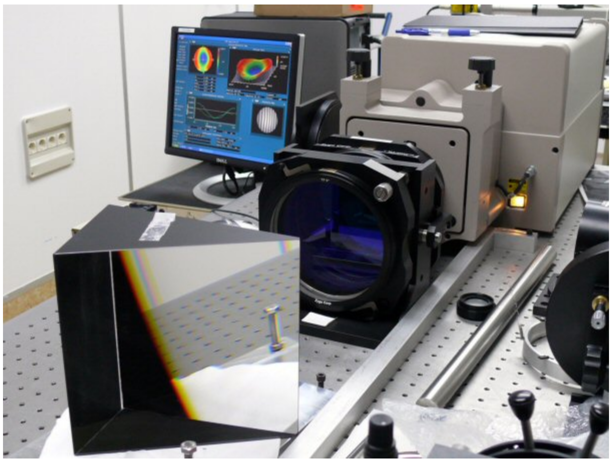

Fig. 8. Test-bench of an interferometer.

The IAC has a significant experience in the management, design and characterization of optical devices to be assembled in sensitive receivers for astrophysical applications.

5 Applicability of the astrophysical differential technological to biomedical applications

The THz technology can be used both in astrophysics and in the medical field, transferring the knowledge between areas. Shortly, a thorough analysis should be performed to adapt the astrophysical technology to medical one, since the final product, budget or protocols to fulfil can slightly differ.

These above mentioned key points, among others, should address to define requirements to be able to transfer technology to the biomedical field, since medical restrictions are mandatory. Furthermore, the maintenance of the developed devices in the medical field is also required in a more exhaustive way than in the astrophysical area.

THz radiation is being employed in the medical field for early diagnosis, cell monitorization and human health care. Considering the technology trends that are currently available, microbolometers operating at the corresponding wavelengths could offer significant results in the biomedical field. As previously mentioned, the high attenuation of the water molecules complicate the measurement of the tissues. Yet the characterization could be complemented by external agents that enhance the overall response and make the measurement feasible.

The commonly used spectroscopy systems requires THz lasers to generate the pulses in the receiver. The lasers employed in these systems are ultrafast devices with a biased photoconductive antenna to properly and effectively produce the THz pulse. Then, it should be collected, collimated and focused onto the sample under test.

Regarding radiometry equipment, telescope instrumentation could also be adapted to biomedical applications. However, the cryogenically cooled technology, often selected in astrophysics, is not appropriate for medical technology. Therefore, the receiver topology should be adapt to operate at ambient temperatures to keep the sensitivity of the systems.

These systems can implement passive measurements of body tissues, implementing alternatives with pyroelectric detectors, among others, able to sensitively measure at this frequency range. Furthermore, this kind of radiometer can be adapt to modulated receivers using a chopper device combined with THz lasers.

The IAC has led several projects in these areas, so its background in the astrophysical instrumentation could tremendously help in the biomedical area. The IAC has developed optical devices to overcome the sensitivity restrictions of the systems, as well as it has been involved in the development of THz radiometric systems.

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