RECENT ADVANCES IN BIO - MOLECULAR IMAGING USING TERAHERTZ WAVE FOR DISEASE DETECTION

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***Abstract:* This paper emphasizes the basic properties of terahertz (THz) waves, which can be employed in the application of bio-molecular imaging. Many of the applications are discussed. The advantages of THz imaging and how it supersedes other imaging methods is also discussed. The material properties and material required for generation of THz, to be used in THz sources and also materials required for THz absorption, are also reviewed. Finally the recent technological developments in generation and absorption of terahertz are discussed.**

***Key words:* Tera Hertz Imaging, Biomolecular Imaging, nano particles**.

I. INTRODUCTION

Tera Hertz Imaging is being used in many applications including Space sciences, molecular spectroscopy, sub-millimeter wave astronomy, remote sensing. Researchers around the world are applying specialized Tera Hertz Technique to disease diagnosis and many biological applications. Countries such as Russia have been involved in sub-millimeter wave biological investigations using specialized backward-wave tubes for over last five decades. Europeans are very strongly involved in this activity through the large research program " THz Bridge".

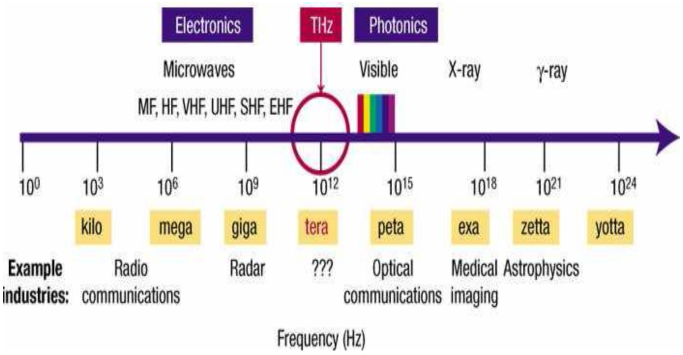

Fig.1:THz Bridge in the frequency Spectrum

Last few years have seen an unprecedented expansion of Tera Hertz components and applications. Popular interest in this unique frequency domain has emerged, spanning applications as diverse as contraband detection and tumor recognition. Use of THz radiation in early detection and diagnosis of Cancer is drawing much attention. The diseased cancerous tissues contain more interstitial water than normal healthy tissues. Also the size of diseased cells is increased and their protein density is also higher as compared to normal cells. This results in higher absorption of THz waves and also higher refractive index of tissues with tumors.

The water level increases in the tumor, which comes from rapid growth of vessels around cancerous cells. This increases contrast in THz imaging for cancer diagnostics **[15]**. But the permeability of THz wave is limited to only measure the surface tissue, resulting in less interaction of THz wave with tissue. This interaction can be increased by reducing the hydration level of fresh tissues.

Early detection of cancerous tissues is very difficult using the methods like computer tomography (CT), magnetic resonance imaging (MRI), or visible and ultrasonic imaging methods. The THz imaging technique is found to be helpful in diagnosis of cancerous tumors. This is because of very low energy levels, due to which it does not cause ionization of tissues or cells. Noticeable changes at a cellular and molecular level have not been found out, even if THz wave exposure intensities reach sub-hundred milli-watt per square centimeter or higher. The conventional THz imaging technique for cancer diagnosis monitors the difference of water concentration or structural change between cancerous tumors and normal tissues. Therefore it is difficult to identify minute differences at the molecular and cellular levels. Therefore it is very necessary to increase the sensitivity and target specificity of THz imaging.

Brief Study of developements in Bio-molecular imaging:

Literature survey was performed to study the existing THz imaging techniques, their advantages, limitations and possible improvements to increase the efficient employment of THz imaging.

II. PROPERTIES OF THZ WAVE

Sub-millimeter wave band (100 µm < λ_o < 1mm) has some basic electromagnetic properties, allowing it's applications to life sciences **[1]**. The energy levels are very low (1-12 meV). Therefore damage to tissues or cells should be limited to generalized thermal effects i.e. strong resonant absorption seems unlikely. Sub-millimeter wavelength scale implies that terahertz signals will pass through tissues with only Mie or Tyndall scattering (proportional to f^2) rather than much stronger Rayleigh scattering (proportional to f^4) that dominates in the IR and optical since cell size is << $\lambda_{o.}$

Two material properties dominate propagation of tera hertz wave in a material, electric susceptibility and bulk conductivity. The over-arching characteristics, as far as terahertz interaction with biological materials is concerned, is absorptive loss due to dielectric polarizability. Broad absorptive loss of terahertz energy is very strong in pure de-ionized liquid water. Things are slightly better in human tissue. Human blood has low frequency resistivity similar to undoped silicon (60-140 Ωcm) and hence would be lossy even without water absorption. Typical tissues (fat, cerebral cortex, liver muscle) have much bulk resistivity (> 1000 Ωcm) at least at megahertz frequencies. Since the materials are really composed of both conducting and non-conducting particles, high frequency values will certainly differ. Considering dielectric loss, some very careful measurements at 120 GHz using high power free electron laser source yielded =75, 71, 79 and 83+/- 3 cm^{-1} for blood, serum, saline solution and culture medium respectively.

The refractive index n of pure water is around 80 at 1 GHz, but drops to around 2 in the sub-millimeter . This gives a reflection coefficient of normally applied terahertz energy that returns about 11% of the incident signal. Due to their water contents, refractive indices of many biological materials change significantly with frequency between 100-1000 GHz. Careful measurements of reflection coefficient versus frequency can, therefore be more useful than absorption in distinguishing tissues.

Since most tissues are immersed in polar liquids, dominated by polar liquids or preserved in polar liquids, the exceptionally high absorption losses at terahertz frequencies make penetration through biological materials of any substantial thickness impossible. However the same high absorption coefficient promotes extreme contrast between substances with lesser or higher degree of water saturation.

One of the hopes for terahertz applications in medical area is in the detection or early characterization of disease, like in identification of dental caries and in examination of skin to access the magnitude and depth of burns. In vivo disease diagnosis is a major driving force for development of hand held and fast scan portable terahertz imaging systems. Skin hydration levels are important for designing percutaneous drug delivery systems, in impacting wound healing, and in accessing the influence of of transpiration on disease or cosmetic appliques. The sensitivity of terahertz signals to skin moisture is very high, and competing techniques like high-resolution MRI are less convenient.

Wound inspections through dressings or solid casts are another promising area that is being investigated with terahertz images. Current techniques use invasive procedures or three dimensional (3D) reconstruction through optical illumination that does not penetrate through opaque bandaging. Terahertz techniques may be able to image, as well as differentiate between different tissue states in the distinct stages of wound closure and scar formation.

A modality that may be of great interest for terahertz systems involves the identification of disease in vascular, bronchial and digestive systems through endoscopy and/or catheter insertion. Differences in the reflection signatures of tissues have already been demonstrated in vivo and there is a fairly good chance that terahertz systems that can be made compact enough to slide into endoscopic or cathetral tubes will be able to distinguish regions of arteriole sclerosis, plaque build up, fat, scar tissue, or other endothelial anomalies.

III. METHODS OF DETECTION

Many methods for detecting the disease or identifying the risk of developing a disease in the future rely on the detection of bio-molecular interactions between a target molecule in the biological sample and a detectable probe molecule **[3]**. The probe molecule is typically identifiable, since it is related and bound to a detectable label. For instance, infection in a subject caused by a infectious agent, such as virus, can be identified by detecting the binding of a labeled antibody probe to a viral protein.

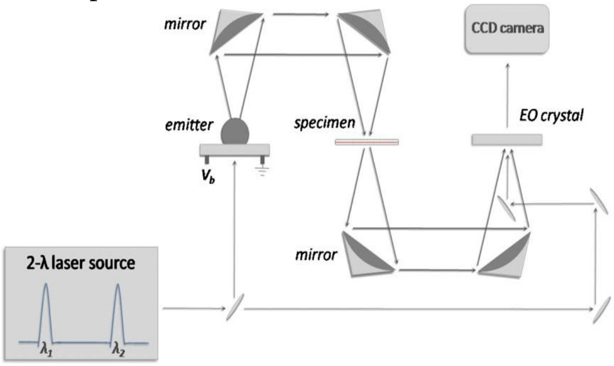

Fig.2: The 2D THz Imaging System

All molecules (biological, organic, inorganic etc.) have inherent rotational and vibrational spectra that lie in the terahertz frequency regime with spectral signature resulting in from intra and inter-molecular interaction. Specific proteins absorb certain characteristic t-ray frequencies, which change their molecular arrangement or conformation leading to a distinct terahertz 'fingerprint' for each bio-molecule, sensors can then detect this absorption revealing the identity of this protein. The 2D THz imaging system is capable of acquiring the absorption and phase coefficients of the specimen across a broad frequency range that extends from 0.3 to 10 THz. It takes advantage of a novel frequency-synthesized THz source that employs a simple frequency tuning mechanism based on the spectral carving of coherent multi-mode optical spectrum. The optical-DFG (Difference Frequency Generator) source was experimentally evaluated in CW (Continuous Wave) operation for different frequencies of the generated DFG signal. The potential of the developed source for pulsed operation was validated through numerical simulations. Terahertz spectroscopic investigations of biological samples have been performed ranging from the simple crystalline form of amino acids, carbohydrates and polypeptides to the more complex aqueous forms of small proteins, DNA and RNA. The vibrationally resolved studies of crystalline samples have revealed the requisite sensitivity of THz modesto crystalline order, temperature, conformational form, peptide sequence and have given unprecedented measures of the binding force constants, properties necessary to improve predictability but not readily obtainable using any other method. THz spectroscopy has enhanced and extended the accessibility to intermolecular forces, length-and timescales important in biological structure and activity.

Sub-millimeter (SMM)/Far Infrared (FIR)/ Terahertz (THZ) region is the most promising region of the electromagnetic spectrum for observing key molecules in space **[4]**. About 130 kinds of molecules have been detected in the interstellar medium. These include many forms of water and organic molecules essential for sustaining life. Approximately one-half of the total luminosity and 98% of the photons emitted since the Big Bang fall into the sub-millimeter and far infrared, THz technology developments is always closely watched by astronomers. Molecular lines are excellent probes of physical and chemical conditions in interstellar clouds, protostar envelopes, circumstellar shells around late-type stars, photon dominated regions etc. In addition, there are also tremendous interests in THz chemical and biological sensing. Furthermore, systems and methods for inspection in biomedical applications, health care and homeland security,, which could detect and define covered damage and pathologic tissues, under skin vessels and organs, target identification of bio and chemical materials, be fast working and suitable in exploitation, are urgently needed in medical science and other fields. Research in moving from simple detection to THz imaging, target identification and location of bio and chemical molecules, has gained tremendous momentum.

Terahertz (THz) imaging has shown promise as the modality of medical diagnostics due to its non invasive nature **[5]**. Conventional THz imaging measures the signal change originating from the variation of interstitial water content or the alteration of a tissue structure. But it cannot distinguish between malignant and benign tumors due to lack of target specificity and the low sensitivity of THz electromagnetic waves to cancerous lesions. The sensitivity of THz imaging can be improved by adopting nanoparticles probes (nanoprobes). Nanoprobes are nano composites that amplify the response of a signal directly or indirectly by using nanoparticles engineered for particular optical, electrical or magnetic properties. They can also be designed to be target specific molecules. The plasmonic resonance induced on the surface of nanoparticles irradiated by near infrared (NIR) waves enhances the sensitivity of terahertz imaging. The surface plasmon resonance raises the ambient temperature of water in cells and tissues and alters the conformational characteristics of water molecules, which results in a stronger THz response. Strengthening of the THz response via nanoprobes facilitates highly sensitive molecular THz imaging (TMI), which is capable of detecting the difference between tumors at the cellular and molecular levels with target specificity. Target specific in vivo images of cancers are obtained using TMI principle.

High sensitivity of TMI was achieved by measuring THz signal change caused by surface plasmon polaritons (SPPs), induced on the surface of metallic nanoprobes under optical beam illumination.

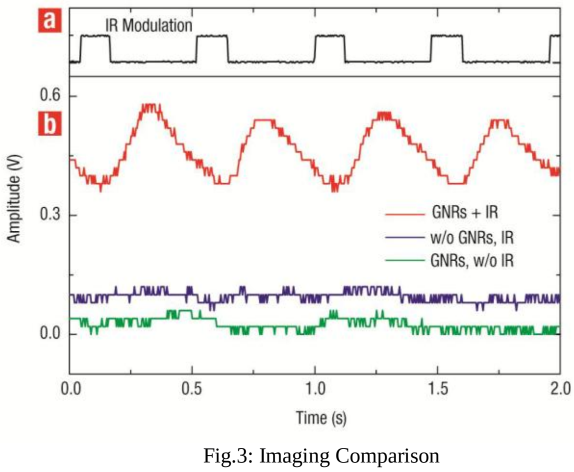

Fig.3: Imaging Comparison

The temperature change was monitored using THz electromagnetic waves to yield TMI signal. The absorption and reflection of THz waves by water depends on the temperature because most of the conformational motions of water correspond to THz range. The temperature sensitivity of THz waves for water is much higher than those of NIR or visible waves. Thus when using TMI, the distribution of minute quantities of nanoprobes can be precisely determined through the measurement of temperature around the nanoprobes. To achieve a more sensitive THz response, the optical beam inducing SPPs is modulated to give differential THz signals responding to heat change only. This differential THz detection technique offers a high contrast image due to exclusive presence of signals from the nanoprobes and highly sensitive nature of THz waves. TMI is sensitive enough to detect 15 micrometer of nanoprobes in vivo, which implies that it is four times more sensitive than the conventional NAI (NIR Absorption Images). TMI proved to be target specific at the cell level, and the cancerous tumors were non-invasively imaged in vivo with high sensitivity and contrast. Thus TMI can facilitate the early diagnosis of cancers, the monitoring of drug delivery processes and the study of biological phenomena at the molecular level.

IV. MATERIAL PROPERTIES

Graphene is a carbon-based, two-dimensional nanomaterial **[6]**. High-quality graphene nanolayers are characterized by a very high carrier mobility, exceeding 20000 $cm^2/V\text{-}s$ and Fermi velocity (v_f) of 10^8 cm/s at low temperatures, as well as excellent thermal and mechanical properties. For these reasons, graphene has been extensively explored as a substrate for radio-frequency (RF) electronics. In parallel, the possibility to to tune the ac conductivity of clean graphene monolayers, and their interesting plasmonic properties at THz frequencies has raised interest in their use in several electrically driven THz optoelectronic and plasmonic devices, including metamaterials, novel frequency-configurable antennas, oscillators etc. The electronic fermi level can be shifted through chemical or electronic doping to control Graphene's sheet conductivity. Recent progress in the growth and lithographic patterning of large-area epitaxial graphene sheet presents great opportunities to realize re-configurable THz optoelectronic and plasmonic devices. THz metamaterials are a class of artificial electromagnetic materials that may enable the realization of interesting electromagnetic devices operating in the THz spectrum, a frequency range in which most natural materials have weak response. Potential applications include efficient generation and sources, lenses, switches, phase and amplitude modulators, beam steering devices and sensors. Thin and tunable graphene metaferrite are potentially low-profile highly efficient absorbers. Another interesting application consists in realizing an artificial magnetic conductor (AMC), which is a composite material that mimics the behavior of perfect magnetic conducting screen. AMC substrates are commonly used at RF to improve the efficiency of radiators, emitters and detectors located close to a ground plane. This graphene metamaterial can provide an alternative design to artificial magnetic structures, realizing a compact THz magnetic substrate.

In the conservative treatment of sufficiently small breast tumors, lumpectomy is the preferred procedure for existing cancerous tissues **[7]**. In this treatment, the tumor is removed via surgery in addition to a few millimeters of healthy tissue surrounding the tumor. The margins of this removed tumor are examined by pathologists via histo-pathological analysis and classified into one of three types. A positive margin indicates that cancerous tissue exceeds the edge of healthy margin; a negative margin indicates that there is no cancerous tissue within 1-2mm of the edge, and a close margin indicates that the cancerous tissue lies less than 1mm of the margin boundary, but does not exceed it. In the case of a positive or close margin identified in the excised tissue, a second surgery is required to remove the remaining cancerous tissue.

Recently, the terahertz (THz) frequency range has been suggested as a potential tool in the use of cancer detection and classification. THz imaging is attractive for its ability to penetrate materials to a depth of several millimeters, giving it an advantage over optical techniques in addressing the concerns. Terahertz waves also lack the polarization energy of x-rays, making them more attractive for in vivo applications, as well as having a higher resolution than microwave imaging. The terahertz range from 0.01THz to 2 THz has been shown to be particularly useful for cancer detection due to noticeable differences in electrical properties between cancerous and healthy tissue in tumors taken from breast and colon. A numerical THz model was used based on discrete dipole approximation (DDSCAT) for investigating the scattering from excised cancerous tissue in the terahertz band. The modeling technique was employed to calculate scattered electric fields from excised breast tumor samples and computer tomography method was implemented to reconstruct the cancer margins. Well known Rytov tomography algorithms were applied to the synthetic simulated data. The scattered fields were calculated using open source DDSCAT at multiple receivers created by multiple incident waves. The DDSCAT was shown to successfully model the scattered electric fields from heterogeneous and irregular tumor patterns. The reconstructed images at 1 THz demonstrate that terahertz technology has potential for the use of tumor margin assessment. The authors suggest that use of a new nonlinear inverse scattering tomography algorithm such as the linear sample method (LSM) would be able to greatly increase the resolution of image reconstruction of breast cancer margins regardless of the contrast between cancerous and normal tissues. Also LSM is not subject to the low permittivity limitations when utilized to determine the contrast of scatterers against the background. In addition, the ongoing research is focusing on measuring the THz fields reflected from ex-vivo breast cancer samples in order to test the new tomography algorithm on experimental data

Mai scattering, HB (Hammerstad and Bekkadal) and full-wave (FEM: Finite Element Method) numerical model have partial success at predicting the effective conductivity in complementary regimes of surface roughness. The first and third methods are comparably effective at predicting the effects of surface topography when the roughness is less than the conventionally estimated skin depth but they overestimate the the surface conductivity when surface roughness exceeds that value. The HB model is effective at predicting the conductivity when the surface roughness exceeds the conventionally estimated skin depth but exaggerates the reduction in conductivity from from surface topography when the roughness is smaller than that value.

The giant tunable Goos-Hanchen shifts in prism/graphene structure were investigated **[9]**. It was found that large positive and negative lateral Goos-Hanchen shifts can be easily controlled by adjusting the chemical potential of graphene, which is modulated by the externally applied electric field. By using the stationary phase method, the effect of externally applied electric field on Goos-Hanchen shifts of proposed prism/graphene structure was theoretically analyzed.

The theoretical studies shows that the magnitude of the Goos-Hanchen shift is more than 200 times that of the operating terahertz wavelength. Numerical calculation results further indicate that the present structure has potential application for the terahertz-wave switch.

Metamaterial-based perfect absorbers have attracted considerable attention due to their potential for practical applications **[10]**. The existing absorbers however are polarization insensitive or only sensitive to one direction, which is inapplicable in some areas. Polarization tunable or high absorption in two orthogonal directions is very useful and necessary.

A polarization tunable absorber presented here is formed by an asymmetric patch and a dielectric layer on the top of a metallic board. With this structure, the frequency of absorber can be tuned by merely changing the polarization of the incident. The tunable mechanism originates from the different length of the patch along the two orthogonal directions. The concept is general and applicable to various absorbers, as long as the asymmetric design is applicable. The absorber can find practical applications in manipulation of the polarization of the light and detecting waves with specific polarization.

This review describes some of most notable advances for THz photonics that took place in 2013 **[11]**. Particularly, the latest results related to high power THz wave generation are reviewed both for time domain broadband sources and monochromatic sources. Also explained are advances in some notable applications.

V. CHALLENGES IN THZ APPLICATIONS

While realizing applications of Terahertz radiation, one of the principal challenges was to develop compact, low-cost, efficient THz sources **[12]**. Development of the THz quantum cascade laser has provided a potential solid state solution. Recently, the THz QCLs have been demonstrated with peak pulsed output powers (P_{peak}) of up to 470 mW per facet, using a direct wafer bonding technique to stack two separate THz QCLs together, thereby increasing the active region and waveguide thickness. In general, increased output powers can be obtained, in the conventional interband semiconductor lasers and mid-infrared QCLs by using longer and broader cavities, with a P_{peak} of up to 120W.

The peak power of the device designed scales linearly with the ridge width. For the devices with a cavity length of 1.5 mm, the scaling factor dL/dw~0.98 mW/ µm, where L is the emitted power, whereas for devices with cavity length of 1 mm, the scaling factor is ~0.60 mW/µm. The effective mirror losses from the device facets, which scale inversely with the cavity length, are likely to be responsible for this difference. Similarly the emitted power scales with the cavity length. A P_{peak} of up to ~780 mW was obtained from a device with 3 mm long cavity and a 425 µm wide ridge.

To increase the emitted power from a specific facet, a high reflectivity coating can be applied to the opposite facet. A P_{peak} of ~ 1.01 W at 10 K is obtained from the front facet, at a frequency of ~3.4 THz, and the device operated to a maximum heat sink temperature of 118 K. With the increasing current, the lasing spectra show a multimode behavior and both broaden significantly and shift to higher frequencies. Owing to the wider ridges, the lateral modes are also present in the lasing spectra.

Graphene, a one-atom-thick planar sheet of sp^2-hybridized orbital bonded honeycomb carbon crystal has unique carrier transport and optical properties **[13]**. The conduction band and valence band of graphene take symmetric conical shape around the K and K' points and contact each other at K and K' points. Electrons and holes in graphene hold a linear dispersion relation with zero band gap, resulting in peculiar features like mass less relativistic Fermions with backscattering-free ultrafast transport and extraordinary electron/hole mobility higher than 200000 cm^2/Vs, as well as the negative-dynamic conductivity in the terahertz spectral range under optical or electrical pumping.

To realize such graphene-based devices, understanding the non equilibrium carrier relaxation/recombination dynamics is crucial. Ultrafast energy relaxation of photo excited carriers by optical phonon (OP) emissions has been predicted. Recently, time-resolved measurements of fast non equilibrium carrier relaxation dynamics have been carried out for multilayers and monolayers of graphene. For electron-hole recombination, optical-phonon-assisted or radiative recombination via direct transition may take place. Carrier-heating effects at high (room) temperatures and/or strong pumping with high photon energy make the carrier dynamics rather complex process that are strongly modified by intraband and interband carrier-carrier scattering.

When we consider the non equilibrium carrier relaxation/recombination dynamics of optically pumped graphene, a very fast energy relaxation of photo-excited electrons/holes via the OP emission and a relatively slow recombination will lead to the population inversion in a wide terahertz range under sufficiently high pumping intensity. This will make it possible to obtain the negative dynamic conductivity or gain in the terahertz spectral range. The possibility of terahertz gain in such systems under cryogenic conditions has been found analytically.

1. Peter H. Siegel in his paper “Terahertz Technology in Biology and Medicine”(IEEE Transactions, Oct 2004) presented survey of some of Terahertz measurements and applications of interest in the biological and medical sciences.
2. Brand M. Fischer and two others in their paper “Terahertz time-domain spectroscopy and imaging of artificial RNA “(OPTICS EXPRESS, 11 July 2005) demonstrated use of terahertz time-domain spectroscopy (THz-TDS) to measure the far-infrared dielectric function of two artificial RNA single strands. They showed that under controlled conditions it is possible to use the THz image to distinguish between two RNA strands.
3. P. Bakopoulos and others in their paper “ A tunable continuous wave (CW) and short-pulse optical source for THz brain imaging applications “ (IOP Publications, September 2009) demonstrated recent advances towards the development of a novel 2D THz imaging system for brain imaging applications, both at the macroscopic and the bio-molecular level. Experimental results confirm the successful generation of THz radiation in the range of 0.2-2 THz, verifying the enhanced frequency tunability properties of the proposed system. Finally the roadmap towards capturing functional brain information by exploring THz imaging technologies is discussed, outlining the unique advantages offered by THz frequencies and their complementarities with existing brain imaging techniques.
4. Hemant Dave and others in their paper “SUBMILLIMETER WAVE SCIENCE AND APPLICATIONS” (Physical Research Laboratory, Ahmadabad 380009, India) present the state-of-art high spectral resolution heterodyne receiver system from 300 GHz to 3 THz range with its possible future applications.
5. Seung Jae Oh and others in their paper “Molecular imaging with terahertz waves” (OPTICS EXPRESS, 28 February 2011) demonstrated a highly sensitive THz Molecular Imaging (TMI) technique involving differential modulation of surface plasmons induced on nanoparticles and obtained target specific in vivo images of cancers. The high thermal sensitivity of TMI can help extend photonic-based photo thermal molecular imaging researchers from the in vitro level to in vivo level.
6. Pai-Yen Chen and one in their paper “ Terahertz Metamaterial Devices Based on Graphene Nanostructures (IEEE Transactions, November 2013) proposed the concept and practical design of THz meta-material devices consisting of subwavelength graphene nanostructures placed on a dielectric substrate and backed by a metal gate. This geometry allows to introduce the design of a THz metaferrite screen with effective permeability that can be tuned from positive to negative, as a function of Graphene’s Fermi energy.
7. T. C. Bowman and two others in their paper “ Imaging 2D Breast Cancer Tumor Margin at Terahertz Frequency using Numerical Field Data based on DDSCAT”(ACES JOURNAL, November 2011) presented tomography of breast cancer tumor margins in the terahertz frequency band. The discrete dipole approximation is employed to calculate the electromagnetic fields scattered from heterogeneous breast tumors. The obtained tomography images demonstrate a potential for terahertz frequency for identifying and assessment of breast cancer tumor margins.
8. Benjamin B. Yang and one in their paper “Theoretical and Empirical Evaluation of Surface Roughness Effects on Conductivity in Terahertz Regime” (IEEE Transactions, May 2014) presented direct measurement of effective conductivity of samples with

periodic controlled roughness features using an open quasi-optical resonator at 400 and 650 GHz. They found that Mai-scattering-based model and finite-element approach are more accurate for samples that are smooth relative to the skin depth. For surface features greater than skin depth, they found that Bekkadal model to be better predictor of effective conductivity.

9. Li Jiu-Sheng and two others in their paper "Giant Tunable Goos-Hanchen Shifts Based on Prism/Graphene Structure in Terahertz Wave Region" (Photonics Journal, IEEE, and November 2014) investigated the giant tunable Goos-Hanchen shifts in prism/graphene structure. They found that large positive and negative lateral Goos-Hanchen shifts can be easily controlled by adjusting the chemical potentials of the graphene, which is modulated by the external applied electric field. By using the stationary-phase method, they theoretically analyzed the effect of externally applied electric field on Goos-Hanchen shifts of proposed prism/graphene structure. Their theoretical study shows that the magnitude of the Goos-Hanchen shift is more than 200 times that of the operating terahertz wavelength. Numerical calculation results further indicate that the present structure has the potential application for the terahertz wave switch.
10. Ben-Xing Wang and others in their paper "Polarization Tunable Terahertz Metamaterial Absorber" (Photonics Journal, IEEE, June 2015) studied the existing Metamaterial based perfect absorbers. They found that the existing absorbers are mostly polarization insensitive or sensitive to one direction, which is inapplicable in some areas. Polarization tunable or high absorption in two orthogonal directions is very useful and necessary. They presented a polarization tunable absorber formed by an asymmetric patch and a dielectric layer on top of a metallic board. With this structure, the frequency of the absorber can be tuned by merely changing polarization of incident. The tunable mechanism originates from the different length of patch along two orthogonal directions.
11. Hermosa Ito in his paper "Breakthroughs in Photonics 2013: Terahertz Wave Photonics", (Photonics Journal, IEEE, March 2014) presents an overview of recent developments in terahertz science and technology. Important advances have occurred in higher power terahertz sources and in other devices. They are described in the paper along with some notable applications.
12. Lianhe Li and seven others in their paper "Terahertz quantum cascade lasers with >1W output powers" (ELECTRONICS LETTERS, Vol. 50, No. 4, February 2014) demonstrated terahertz (THz) frequency quantum cascade lasers emitting peak powers of >1W from a single facet in the pulsed mode. The active region was biased on a bound-to-continuum transition with a one-well injector, and was embedded into a surface-plasmon waveguide. The lasers emitted at a frequency of ~3.4 THz and had a maximum operating temperature of 123 K. The maximum emitted powers were ~1.01 W at 10 K and ~420 mW at 77 K, with no correction made to allow for the optical collection efficiency of the apparatus.
13. Taiichi Otsuji and two others in their paper "Terahertz-Wave Generation Using Graphene: Towards New Types of Terahertz Lasers" (Accepted in IEEE Journal of selected topics in Quantum Electronics) review recent advances in terahertz wave generation in graphene towards the creation of new types of terahertz lasers. First, fundamental basis of the optoelectronic properties of graphene was introduced. Then the paper describes non equilibrium carrier relaxation and recombination

dynamics in optically and electrically pumped graphene to introduce a possibility of negative dynamic conductivity in wide terahertz range. Then recent theoretical advances toward the creation of current-injection graphene terahertz lasers are described. Next unique terahertz dynamics of 2-D plasmons in graphene are described. Finally the paper summarizes the advantages of graphene materials and devices for terahertz wave generation.

14. P. Kung and S. M. Kim in their paper "Terahertz Metamaterial Absorbers for Sensing and Imaging" (PIERS Proceedings, Taipei, March 2013) present the design and finite element simulation of thin, tunable, polarization insensitive metamaterial terahertz absorbers. They propose a novel metamaterial structure with a broadened bandwidth of absorption in the THz. This concept was based on multiple band absorption and was achieved by bringing bands close enough to one another in a multi-layered pattern, which decreases the negative interaction between rings and corresponding resonators.

VI. CONCLUSION AND FUTURE WORK

All molecules (biological, organic, inorganic etc.) have inherent rotational and vibrational spectra that lie in the terahertz frequency regime. Tera Hertz Imaging is being used in Space sciences, molecular spectroscopy, sub-millimeter wave astronomy, remote sensing.

We have reviewed the properties of terahertz radiation. Due to its very low power level, THz waves are better suitable for biomolecular imaging, as compared to other techniques. In other techniques, they cause harm to human tissue, if *in vivo* imaging is required. Otherwise detecting abnormality in human tissues is very difficult and requires a long time. The exceptionally high absorption losses at terahertz frequencies make penetration through biological materials of any substantial thickness impossible. However the same high absorption coefficient promotes extreme contrast between substances with lesser or higher degree of water saturation. Wound inspections through dressings or solid casts can also be efficiently done using THz imaging.

Terahertz Molecular Imaging sensitivity can be highly increased by injecting metallic nanoprobes. The surface plasmon polaritons induced on the surface of metallic nanoprobes result in change of THz signal. The absorption and reflection of THz waves by water depends on temperature because most of conformational motions of water correspond to THz range. Thus when using TMI, the distribution of minute quantities of nanoprobes can be precisely determined through measurement of temperature around the nanoprobes.

The review also shows graphene to be suitable material to be used in THz sources. Also many imaging techniques have been reviewed.

We, therefore propose use of nanoparticles in Terahertz Molecular Imaging. A suitable material for nanoparticles is to be found that will provide maximum sensitivity to TMI. Also proper shape and size of nanoparticles is to be obtained to maximize the TMI. Temperature of abnormal cells in human tissue is different from temperature of normal cells. This difference of temperature can be used for early detection of Cancer in human tissue, using TMI, enhanced by nanoparticles.

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