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RECENT ADVANCES IN TERAHERTZ TECHNOLOGY FOR SECURITY AND BIOMEDICAL APPLICATIONS

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Abstract. Terahertz waves have low photon energies (~ 4.1 meV for 1 THz), which is about 1 million times weaker than the energy of X-ray photons. They do not cause any harmful ionization in biological tissues. The terahertz radiation is strongly attenuated by water and is very sensitive to water content. This paper provides current status and recent advances in terahertz technology for security and medical applications. In particular, we report on our designs of THz quantum cascade lasers to identify cancerous tissues and other medical issues.

Rezumat. Undele Terahertz au energii fotonice scăzute (~ 4,1 meV pentru 1 THz), care este de aproximativ 1 milion de ori mai slabă decât energia fotonilor cu raze X. Ele nu provoacă nicio ionizare dăunătoare în țesuturile biologice. Radiația terahertz este puternic atenuată de apă și este foarte sensibilă la conținutul de apă. Această lucrare oferă starea actuală și progresele recente în tehnologia terahertz pentru aplicații de securitate și medicale. În special, raportăm despre proiectele noastre de lasere cu cascadă cuantică THz pentru a identifica țesuturile canceroase și alte probleme medicale.

Keywords: terahertz radiation; medical applications; quantum cascade lasers; zinc oxide, zinc selenide.
Cuvinte cheie: radiații terahertz; aplicații medicale; lasere cu cascadă cuantice; oxid de zinc, selenură de zinc.

Introduction

Terahertz (THz) waves refer to the electromagnetic radiation in the frequency range from 0.1 to 10 THz, which corresponds to the wavelengths from 3 mm to 30 μm, respectively [1-5]. This spectral region, called also "T-gap", is important for many practical applications, including THz imaging, chemical and biological sensing, high-speed telecommunication, security, and medical applications [5-14]. THz waves have low photon energies (~ 4.1 meV for 1 THz), which is about 1 million times weaker than the energy of X-ray photons, they neither ignite any explosive materials at typical power levels nor cause any harmful ionization in biological tissues [2]. Thus, THz waves can be considered as a safe method for investigation of biological materials and which can be used in medicine for THz imaging and for other applications.

Terahertz quantum cascade lasers (THz QCLs) have a very narrow spectral line with a linewidth of ~ 31 kHz [3], which is very important for THz spectroscopy. Despite the great progress made in the last few years in the design, fabrication and demonstration of THz QCLs based on AlGaAs/GaAs materials [6], there are some limits of bandgap engineering due to the relatively low conduction band offset (CBO) (0.72 eV for GaAs/AlAs). This, in particular, means that THz generation cannot be obtained at room temperature, as required for many of the applications envisaged. It is therefore important to consider other compound semiconductors, in particular InAlGaN/GaN, SiGe/Si ZnMgSe/ZnSe, and ZnMgO/ZnO material systems [7-20]. The two latter systems are suitable for room-temperature THz sources. Below we review the recent progress and current status of terahertz technology for security and biomedical applications.

THz spectroscopy for security applications

THz spectral region covers intermolecular vibrations of biological molecules and low frequency crystalline lattice vibrations of chemical materials, including drugs, explosive and related compounds (ERCs) such as TNT, RDX, HMX, PETN and other explosive materials [2, 4]. Transmitted and reflectance THz spectra of these materials contain specific THz absorption peaks (finger-prints), which characterize vibration modes of these materials and provide information which could be used for the identification of the explosives, which is not available in the other regions of the electromagnetic spectrum. Since most tunable THz sources produce only small power levels, we propose for routine evaluation of dangerous materials to employ a chain of quantum cascade THz generators, where each of them addresses a specific spectroscopic line of the relevant identifying spectrum. We suggested structure and design of a room-temperature monolithic broadband terahertz (THz) source for applications of THz imaging and detection of explosive materials [7]. The suggested terahertz source is a 20-element array of quantum cascade lasers (QCLs) emitting at discrete frequencies from 0.85 to 4.74 THz. The layer structure of each individual THz QCL is based on a two-well design scheme with variable barrier heights and resonant-phonon depopulation of the lower laser state. The tailoring of emission frequency of individual THz QCLs in the laser array was made by varying the constituent epilayers’ width and doping level of the injector well. We found that the peak optical gain of the discrete THz QCLs is increased with increasing tailored THz emission frequency. The detection of the transmitted line can be done by THz Schottky diodes after relevant narrow-band filters.

THz spectroscopy for medical applications

In the last two decades THz spectroscopy has been widely used to probe and characterize various biomolecules because most low-frequency biomolecular motions, including vibration and rotation of the molecular skeletons, lie in the same frequency range as THz radiation. Therefore, various molecules can be clearly identified and characterized according to their spectral fingerprints. One example of potential clinical applications of this frequency range is reported in Moreno-Oyervides et al. [21] where with the help of advanced statistical techniques (functional data analysis) they used a W-band (75-110 GHz) spectrometer for the non-invasive detection of hyperglycemic states in mice.

The 20 naturally-occurring amino acids have an absorption characteristic in the 1–15 THz range. Kutteruf et al. [22] reported THz absorption spectra of solid phase peptides at 77 K and 298 K and proved that the structure information of a short peptide chain in the range of the 1–15 THz band was highly consistent with the measured spectral information. It was observed that, as the temperature decreased, the absorption peak of the peptide chain became sharper. It is established that with an increase in the number of amino acids, the peptide absorption lines became complicated, the density and uniqueness of different absorption peaks predicted the correlation between THz spectrum and the sequence structure.

Terahertz spectroscopy is one of the fast and non-invasive method for the detection of wide range viruses, including the Zika virus, H5N2, H1N1, H9N2 and COVID-19. COVID-

19 belongs to the Corona family of viruses. It has a virus particle size about 125 nm and consists of 3 proteins: protein E, the membrane protein M and the glycoprotein Spike S. Recently, Ahmadivand et al. [23] reported the successful development of a THz plasmonic biosensor device based on toroidal dipole-resonant metamolecules. Their devices demonstrate extreme sensitivity to the presence of SARS-CoV-2 spike protein, which allowed to detect the presence of spike protein with significantly low LoD ~4.2 fmol.

The early detection of cancer is one of the most important issues in medical diagnosis because it provides a possibility to treat cancer before it grows too large and spreads to other organs [24]. Among different types of techniques, terahertz spectroscopy shows a high sensitivity for chemical and structural changes in biological molecules without causing ionization, due to its low photon energy. Carcinogenesis involves the structural and chemical alteration of biomolecules in cells. Aberrant methylation of DNA is a well-known carcinogenic mechanism. Terahertz waves can directly observe changes in DNA because the characteristic energies lie in the same spectral region. The authors of [25] reported on terahertz molecular resonance fingerprints of DNA methylation in cancer DNA. They detected THz molecular resonance fingerprints caused by the methylation of cancer DNA extracted from living cell lines and quantified them to distinguish cancer types. Two major absorption peaks (1.29 THz and 1.74 THz) for methylation were identified between 0.4 THz and 2.0 THz by comparing two nucleoside samples, 2′-deoxycytidine (2′-dC) and 5-methylcytidine (5-mC), as well as chemical analogues.

ZnSe- and ZnO-based terahertz quantum cascade lasers

We have numerically investigated ZnMgSe/ZnSe- and ZnMgO/ZnO-based THz QCLs with different design schemes. The structure of these QCLs are based on 2-well and 3-well design schemes with diagonal laser transitions, employing resonant-tunneling and intra-well depopulation of lower laser state mechanisms. As reference, we have chosen the design of ZnMgO/ZnO THz QCL suggested by Bellotti et al. [26], which consists of three ZnO quantum wells and $Zn_{0.85}Mg_{0.15}O$ quantum barriers. The layer thicknesses of one cascade of such a QCL starting from the injector barrier in nm is: **3.0**/3.1/**2.5**/2.4/ **3.4**/$\underline{5.5}$, where the underlined quantum well is homogeneously n-type doped with a concentration of 3×10^{16} cm^{-3}.

Our approach for high-power room-temperature ZnMgSe/ZnSe- and ZnMgO/ZnO-based THz QCLs are based on a 2-well design scheme employing the fixed and variable barrier heights and a delta-doped injector. The layer thicknesses of one cascade of investigated QCLs employing 2-well design schemes with fixed and variable barrier heights starting from injector well in nm are equal to **3.1/**$\underline{6.2}$**/1.7/**12.9 and **2.7/**$\underline{6.2}$**/1.5/**11.9 for ZnSe-based QCLs, and are equal to **2.7**/$\underline{6.0}$/**2.6**/4.0 and **2.7**/$\underline{6.2}$/**1.5**/11.9 for ZnO-based QCLs, respectively. The underlined quantum well were homogeneously n-type doped with a concentration of 1×10^{18} cm^{-3} (for QCLs with fixed barrier heights) and were delta-doped with a concentration of 1×10^{18} cm^{-3} (for QCLs with variable barrier heights). The ZnSe-based QCL with fixed barriers consist of $Zn_{0.76}Mg_{0.24}O$ quantum barriers and ZnSe quantum wells, while devices based on a design with variable barrier heights consist of $Zn_{0.80}Mg_{0.20}Se$ and $Zn_{0.70}Mg_{0.30}Se$ quantum barriers and ZnSe quantum wells. The ZnO-based QCL with fixed barriers consist of $Zn_{0.85}Mg_{0.15}O$ quantum barriers and ZnO quantum wells, while devices based on a design with variable barrier heights consist of $Zn_{0.90}Mg_{0.10}O$ and $Zn_{0.80}Mg_{0.20}O$ quantum barriers and ZnO quantum wells. The material parameters were taken from [7-20]. For comparison, we have also simulated the best experimental $Al_{0.15}Ga_{0.85}As$/GaAs THz QCL [6]. The calculated radiation frequency of this device at 200 K is 3.50 THz, slightly higher than the experimental value of 3.22 THz. Thus, these results confirm the validity of the used model and software.

It was established that among all devices, at room temperature the best value of optical gain of 108 cm^{-1} @ 2.18 THz is given by the ZnMgO/ZnO THz QCL with a 2-well design scheme and variable barrier heights. This value is significantly higher than the performance of the other devices: 60 cm^{-1} @ 3.13 THz for ZnMgO/ZnO THz QCL with a 2-well design scheme and fixed barrier heights, 1.4 @ 7.13 THz for ZnMgO/ZnO THz QCL with a 3-well design scheme and fixed barrier heights, 37 cm^{-1} @ 1.33 THz for ZnMgSe/ZnSe THz QCL with a 2-well design scheme and fixed barrier heights, and ~ -200 cm^{-1} (is negative) for ZnMgSe/ZnSe THz QCL with a 2-well design scheme and fixed barrier heights. The higher laser performance of ZnMgO/ZnO THz QCLs compared with AlGaAs/GaAs is attributed to the higher LO-phonon energy in ZnO (72 meV for ZnO vs. 36 meV for GaAs). The suggested approach of THz QCL devices with 2-well design scheme employing alternating variable barrier heights leads to the enhancement of optical gain and also reduces thermally activated carrier leakages via higher-energy parasitic levels [9].

Conclusion

Finally, we can conclude that THz technology has made remarkable progress. In addition, it shows great potential for security and biomedical applications, already under development, such as label-free pathogen identification. However, some challenges must be overcome, because the strong absorption of water throughout the THz frequency range has been a huge obstacle to biological detection. The THz signal of water is stronger than that of biomolecules, thus impairing accurate detection.

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