

The possibility of using quantum cascade lasers for terahertz absorption spectroscopy of samples of biological origin

© V.L. Vaks^{1,2}, V.A. Anfertev^{1,2}, E.G. Domracheva¹, V.I. Gavrilenko^{1,2}, M.B. Chernyaeva¹

¹ Institute of Physics of Microstructures, Russian Academy of Sciences, Nizhny Novgorod, Russia

² Ioffe Institute, St. Petersburg, Russia

E-mail: elena@ipm.sci-nnov.ru

Received October 6, 2025

Revised December 9, 2025

Accepted December 9, 2025

The extension of high-resolution gas spectroscopy in the terahertz range is associated with developing tunable highly stable sources of radiation, for instance, quantum cascade lasers. The paper presents the results of examining the possibility of using a quantum cascade laser (3.8 THz) to study a mixture of vapors and products of thermal decomposition of biological fluid (urine). Examples of measuring the lines of water and isocyanic acid that lie within the quantum cascade laser tuning range are given. The presented results demonstrate the prospects of using the quantum cascade laser to create a line of lasers for studying biological samples.

Keywords: quantum cascade laser, high-resolution spectroscopy, absorption line, metabolite-marker.

DOI: 10.61011/TPL.2026.04.63202.20518

Due to peculiar features of terahertz (THz) radiation and its interaction with matter, the number of publications related to the THz radiation application in biology and medicine is currently growing. Those publications are mainly devoted to THz time-domain spectroscopy [1], as well as to creating THz-imaging systems and using them to visualize pathologically altered tissues [2,3]. However, a promising approach for diagnostic purposes is metabolic analysis [4] with identifying characteristic absorption lines of metabolite-markers for pathological conditions in the spectra of biological samples under study. This approach is being developed at IPM RAS by using the methods of non-stationary terahertz gas spectroscopy and is being successfully applied, e.g., in the THz range low-frequency part for studying biological fluids (urine, blood), tissues (organ tumors), etc. [5]. For the higher frequency range, the results of spectroscopic studies of biological fluids (including urine) have not been yet reported in literature.

Lines of the substance rotational absorption spectrum lie in the frequency range overlapping the intervals from a few GHz to several THz and have different intensities in different parts of the spectrum. For example, integrated intensities of the isocyanic acid absorption lines in the 2-mm range are about $10^{-3.0279} - 10^{-5.3043} \text{ nm}^2 \cdot \text{MHz}$ (131–164 GHz); with increasing frequency, the integrated intensities increase and reach the maximum in the THz range of $10^{-0.9283} - 10^{-1.7203} \text{ nm}^2 \cdot \text{MHz}$ (near 2.623–2.667 THz) [6,7]; therefore, in detecting individual compounds, transition to the terahertz frequency range allows increasing the sensitivity of detecting the substances contained in the gas mixtures under study.

To move into the higher frequency range and make it possible to use high-resolution spectroscopy, narrow-band tunable radiation sources are required. Promising

sources of THz-range radiation are quantum cascade lasers (QCLs) [8]. QCLs are unipolar semiconductor lasers based on intersubband optical transitions in heterostructures. They are able to operate both in the continuous and pulsed modes and provide sufficiently high power required for applications where such sources may be used (e.g. spectroscopy and its application in various fields, such as medicine, biology, THz imaging, wireless communications, etc.). In the infrared range, QCLs operate at room temperature and serve as radiation sources for medical and biological research (e.g. in studying exhaled air of patients with socially significant diseases: type 1 diabetes mellitus, pneumonia, asthma) [9]. In the THz range, QCLs operate under cryogenic cooling; therefore, spectroscopic studies with QCL-based radiation sources are more complex and are being developed much slower [10].

The goal of this work was to examine the possibility of using a terahertz QCL as a radiation source for studying a biological fluid (urine).

As the radiation source, a pulsed QCL with the resonant phonon design based on three quantum wells per heterostructure period was used [11]. Laser stripes 172 μm wide and 2 mm long with a surface-plasmon waveguide [8] and Fabry–Perot cavity on cleavages were obtained from an molecular-beam epitaxy-grown heterostructure with an active region about 10 μm thick. Frequency characteristics were investigated in [12] by using a high-Q Fabry–Perot cavity. All the measurements were performed at $T = 10 \text{ K}$.

Fig. 1, *a* presents typical emission spectra of two QCL samples fabricated in a single production process on a single substrate; the spectra contain lines corresponding to several longitudinal modes of the laser Fabry–Perot cavity near 3.8 THz. Since the laser operates on diagonal optical transitions between the quantum confined levels in

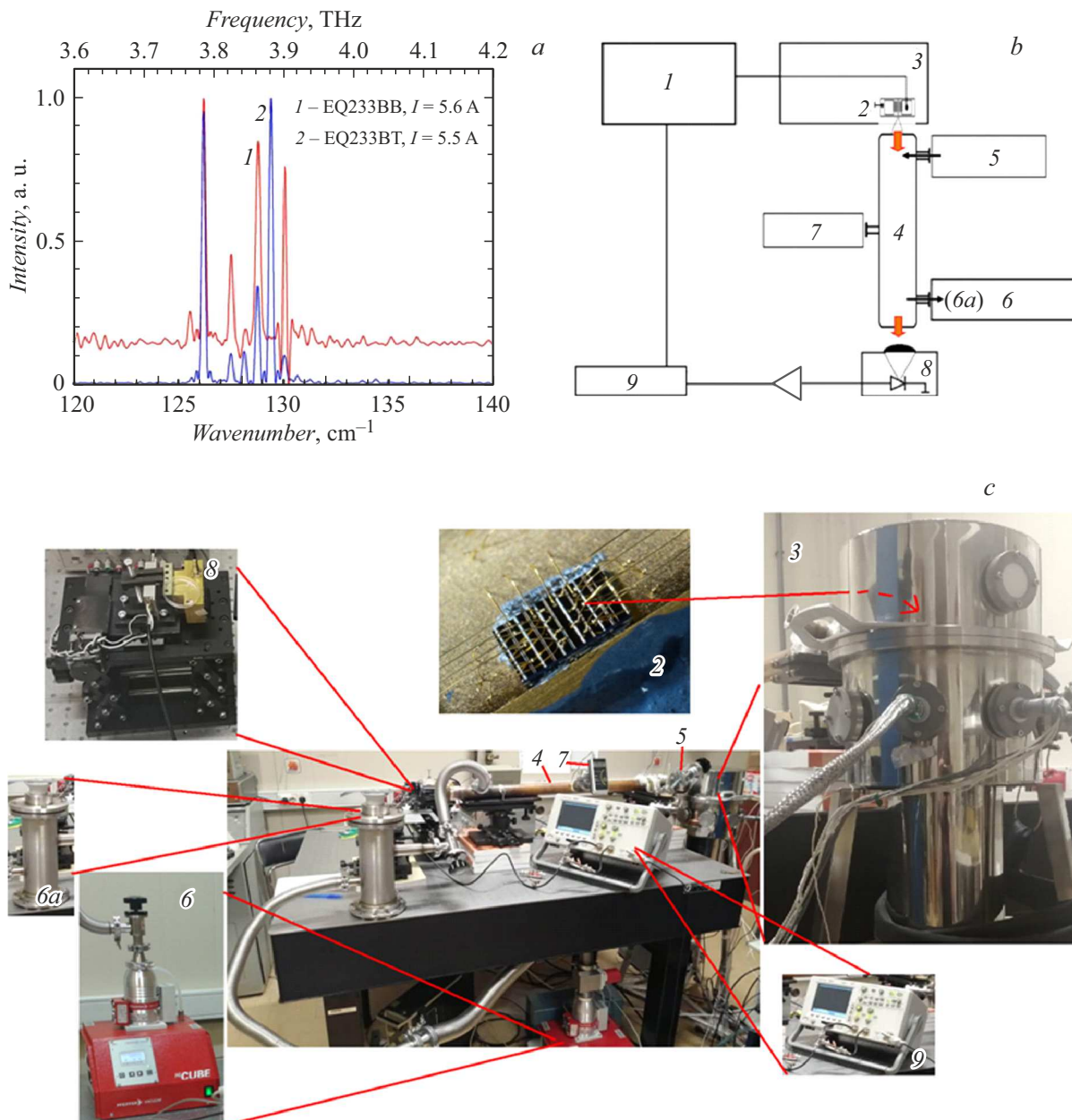


Figure 1. *a* — emission spectra of two QCL samples, *b* — schematic diagram of the spectroscopic setup based on the terahertz QCL (vertical arrows represent THz radiation, black horizontal arrows indicate feeding and evacuation of the gas mixture under study), *c* — a photograph of the spectroscopic setup with individual blocks. 1 — pulse power supply, 2 — QCL, 3 — cryocooler, 4 — measuring cell, 5 — gas mixture inlet system, 6 — vacuum pump station Pfeiffer HiCube 80 Eco with a nitrogen trap (6a), 7 — pressure sensor, 8 — Schottky diode detector, 9 — oscilloscope.

adjacent quantum wells, oscillation frequencies of the used QCL may be slightly adjusted to the absorption line of the studied gas by varying the applied voltage/QCL current based on the well-known effect of the mode frequency „pulling“ [13]. During the pulse, the mode frequency tuning rate is about $500 \text{ MHz}/\mu\text{s}$ [12], which allows sweeping the radiation frequency when one of the modes passes through the studied gas absorption line.

Since QCL can operate in many frequency ranges (Fig. 1, *a*), prior to measurements it was characterized at

the testbench developed earlier at IPM RAS [14]. The test showed that under the specified conditions the laser operating frequency is about 3.80 THz.

After that, there was created a laboratory model of the setup for spectroscopic measurements of multicomponent gas mixtures of biological origin (exhaled air and vapors of biological fluids) (Fig. 1, *b, c*). QCL was installed on the plate of a closed-loop optical cryostat (a Gifford–McMahon helium refrigerator); the measurements were carried out at the cryostat temperature of 10 K. As the detector, a

Schottky diode was used [11]. The QCL radiation pulses were about $7.5 \mu\text{s}$ long at the repetition rate of 1 kHz.

Test measurements were carried out using as an example the 3.7983 THz water vapor absorption line (with the central frequency $f_{cat} = 3\,798\,281.638$ MHz as per the catalog [7]). The results of test measurements of the 3.7983 THz water line at various pressures (0.001–3.1 mbar) are shown in Fig. 2. The cell was first evacuated with vacuum pump Pfeiffer HiCube 80 Eco to the pressure of 10^{-4} mbar and then filled with water vapor to various pressures. To prevent excess water vapor from entering the pump, a nitrogen trap was placed between the cell and pump (Fig. 1). The detector recorded, in the direct detection mode, the signal that has passed during the pulse through the cell containing the studied gas, which ensured coverage of the relevant frequency range of molecules' interaction if their absorption lines fall within it. Actually, during the pulse the frequency retuning takes place, however, since it is highly uneven, the abscissa axis is left in the time domain.

Sensitivity of the model laboratory spectrometer allows for detecting gases at pressures not lower than 1 mbar.

Biological samples were studied by using a previously developed sample preparation technique that has been successfully applied in measurements in the 2-millimeter range; the technique involves cryogenic dehydration of the sample and subsequent heating of the residue along with introducing the residue vapors and thermal decomposition products into the measuring cell [15].

Test measurements of the biological fluid (urine) vapors were carried out. Preliminary measurements of urine vapors and thermal decomposition products performed in the 2-millimeter wavelength range on a fast frequency sweep spectrometer with a radiation source based on a backward-wave oscillator (118–175 GHz) [16] revealed characteristic substances contained in urine samples under heating at an operating pressure of about 0.05–0.1 mbar. Any urine sample (taken from conditionally healthy volunteers, patients

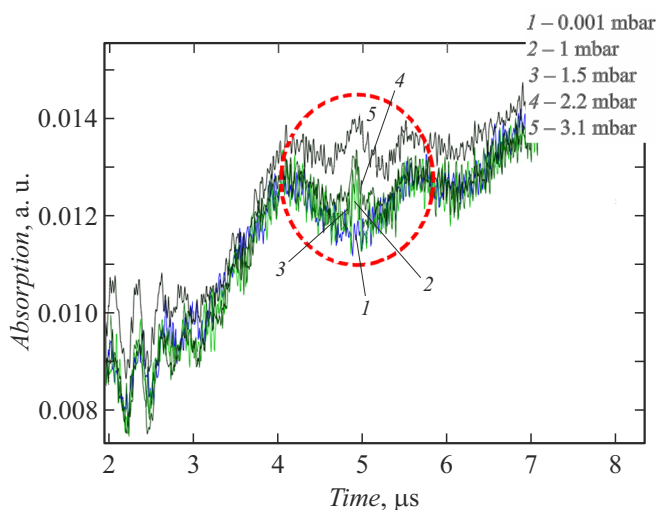


Figure 2. Test measurements of the water line with central frequency of 3.7983 THz for different measuring cell pressures.

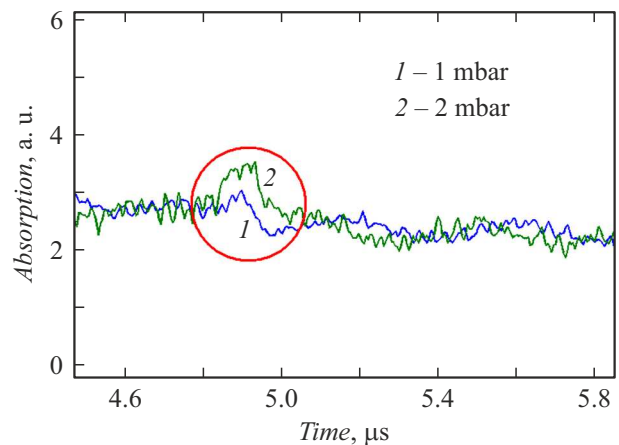


Figure 3. The spectral range containing the HNCO absorption line with the experimentally obtained central frequency $f_{exp} = 3.802$ THz in a mixture of urine vapors and thermal decomposition products at the cell pressure of 1 and 2 mbar.

with adenoma, patients with prostate cancer) exhibits lines of isocyanic acid (HNCO). The HNCO spectrum is known and presented in catalogues [6,7]; the lines indicated in [6] and actually recorded by the 2-mm range spectrometer are envelopes of series of lines given in [7] which are closer than allowed by the resolution of a high-resolution non-stationary spectrometer at the operating pressure and room temperature; this is caused by line spreading due to the pressure of the studied gas mixture in the measuring cell and Doppler broadening.

The QCL tuning range includes the HNCO absorption line. Fig. 3 presents an example of recording the HNCO absorption line near 3.802 THz (with the following spectroscopic characteristics: central frequency $f_{cat} = 3\,802\,074.9669$ MHz as per catalogues, $\lg I = -1.2609$ (where $I[\text{nm}^2 \cdot \text{MHz}]$ is the integrated line intensity) for the transition characterized by quantum numbers 20, 3, 18 \leftarrow 21, 2, 19 [6]) in the mixture of vapors and thermal decomposition products of urine taken from a conditionally healthy volunteer.

Recording the two above-mentioned absorption lines of water and isocyanic acid and knowing the absorption spectra of these substances in the THz range from catalogues, as well as knowing the approximate QCL tuning limits, allows confirming the QCL tuning limits independently of measurements obtained on the testbench (measuring cavity).

Based on the results of spectroscopic studies, we may conclude that it is possible to detect the substances' absorption lines lying in the QCL tuning range, e.g. those of some biologically significant molecules contained in vapors and thermal decomposition products of biological fluids (urine). Later this approach may be used to detect molecules whose spectral lines lie in this part of the THz range, including those of samples of biological origin. And, although retuning of an individual QCL is insignificant (± 2 GHz for QCL under study), the QCL generation range is determined

by the QCL heterostructure design (thicknesses of the heterostructure layers), and it is possible to create a line of QCLs operating in the ranges containing absorption lines of significant metabolite markers.

The results presented demonstrate the potential of employing QCLs in studying vapors and thermal decomposition products of biological samples, which shows the possibility of using this approach for medical applications.

Funding

Investigation of the QCL characteristics was supported by the Russian Science Foundation, project No 21-72-30020-P (<https://rscf.ru/project/21-72-30020/>); QCL-based investigation of vapors and thermal decomposition products of biological samples was performed in the framework of Research Program of the National Center of Physics and Mathematics (project „Physics of High Energy Densities. Stage 2023–2025“).

Compliance with ethical standards

All the procedures performed in studies involving human participants complied with ethical standards of the institutional and/or national research ethics committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. Informed voluntary consent was obtained from each participant involved in the study.

Conflict of interests

The authors declare that they have no conflict of interests.

References

- [1] A.A. Angeluts, A.V. Balakin, M.G. Evdokimov, M.N. Esaulkov, M.M. Nazarov, I.A. Ozheredov, D.A. Sapozhnikov, P.M. Solyankin, O.P. Cherkasova, A.P. Shkurinov, *Quantum Electron.*, **44** (7), 614 (2014). DOI: 10.1070/QE2014v044n07ABEH015565.
- [2] T. Amini, F. Jahangiri, Z. Ameri, M.A. Hemmatian, *J. Lasers Med. Sci.*, **12**, e92 (2021). DOI: 10.34172/jlms.2021.92
- [3] M. Wan, J.J. Healy, J.T. Sheridan, *Opt. Laser Technol.*, **122**, 105859 (2020). DOI: 10.1016/j.optlastec.2019.105859
- [4] D.S. Wishart, Y.D. Feunang, A. Marcu, A.Ch. Guo, K. Liang, R.V. Fresno, T. Sajed, D. Johnson, C. Li, N. Karu, Z. Sayeeda, E. Lo, N. Assempour, M. Berjanskii, S. Singhal, D. Arndt, Y. Liang, H. Badran, J. Grant, A. Serra-Cayuela, Y. Liu, R. Mandal, V. Neveu, A. Pon, C. Knox, M. Wilson, C. Manach, A. Scalbert, *Nucl. Acids Res.*, **46** (D1), D608 (2018). DOI: 10.1093/nar/gkx1089
- [5] V.L. Vaks, E.G. Domracheva, M.B. Chernyaeva, V.A. Anfertev, A.A. Ayzenshtadt, A.V. Maslennikova, V.A. Atduev, *v kn.: Teragertsovaya fotonika*, pod red. V.Ya. Panchenko, A.P. Shkurinova (Izd-vo RAN, M., 2023), s. 576–632. (in Russian)
- [6] C.P. Endres, S. Schlemmer, P. Schilke, J. Stutzki, H.S.P. Müller, *J. Mol. Spectrosc.*, **327**, 95 (2016). DOI: 10.1016/j.jms.2016.03.005
- [7] H.M. Pickett, R.L. Poynter, E.A. Cohen, M.L. Delitsky, J.C. Pearson, H.S.P. Muller, *J. Quant. Spectrosc. Radiat. Transfer*, **60** (5), 883 (1998). DOI: 10.1016/S0022-4073(98)00091-0a
- [8] B.S. Williams, *Nature Photon.*, **1** (9), 517 (2007). DOI: 10.1038/nphoton.2007.166
- [9] I.S. Golyak, D.R. Anfimov, P.P. Demkin, P.V. Berezanskiy, O.A. Nebritova, A.N. Morozov, I.L. Fufurin, *J. Biophotonics*, **17**, e202400151 (2024). DOI: 10.1002/jbio.202400151
- [10] J. Radovanović, N. Vuković, N. Stanojević, A. Demić, M. Stojković, M. Ignjatović, N. Basta, F. Perišić, D. Indjin, *Proc. SPIE*, **13335**, 1333504 (2025). DOI: 10.1117/12.3044671
- [11] S. Kumar, Q. Hu, J.L. Reno, *Appl. Phys. Lett.*, **94**, 131105 (2009). DOI: 10.1063/1.3114418
- [12] V.L. Vaks, V.A. Anfertev, M.B. Chernyaeva, E.G. Domracheva, S.I. Pripolzin, A.N. Baranov, R. Teissier, A.A. Ayzenshtadt, K.A. Gavrilova, *Radiophys. Quantum Electron.*, **65** (10), 760 (2023). DOI: 10.1007/s11141-023-10255-x.
- [13] L. Schrottke, X. Lü, B. Röben, K. Biermann, M. Wienold, H. Richter, H.-W. Hübers, H.T. Grahn, *J. Appl. Phys.*, **123**, 213102 (2018). DOI: 10.1063/1.5024480
- [14] V.A. Anfertev, V.L. Vaks, A.I. REutov, A.N. Baranov, R. Teissier, *Zhurn. radioelektroniki [elektronnyi zhurnal]*, No 12 (2018). DOI: 10.30898/1684-1719.2018.12.5 (in Russian)
- [15] V.L. Vaks, E.G. Domracheva, M.B. Chernyaeva, V.A. Anfertev, A.V. Maslennikova, A.V. Zheleznyak, T.D. Knyazeva, M.A. Rodionov, A.I. Maiorov, *J. Opt. Technol.*, **89** (4), 243 (2022). DOI: 10.1364/JOT.89.000243.
- [16] V. Vaks, E. Domracheva, M. Chernyaeva, V. Anfertev, A. Maslennikova, V. Atduev, K. Atduev, M. Rodionov, *Appl. Sci.*, **14**, 1955 (2024). DOI: 10.3390/app14051955

Translated by EgoTranslating