A Problem of THz Endoscopy of Hard-to-Access Tissues

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Abstract. Despite terahertz (THz) technologies offer a number of applications in medical diagnosis and therapy, their translation into clinics is hampered by the lack of THz endoscopes capable of sensing THz response of hard-to-access tissues. In this paper, we focus on recent attempts to mitigate this difficulty. We consider the two existing principles of THz endoscopy. The first uses the fiber-coupled THz photoconductive antennas (PCAs) for the THz generation and detection in close proximity to an object. The second relies on the THz optical fibers to deliver THz waves to an analyte and then to detect the reflected THz signal. Most recent developments in the area of THz fiber optics pave the way to solve the challenging problem of THz endoscopy. Among them, we emphasize the THz fibers, fiber bundles, waveguides, and endoscopes developed by our research group based on the sapphire shaped crystals obtained by the edge-defined film-fed growth (EFG) technique.

Keywords: THz technology; THz fiber optics; THz endoscopy; THz medical diagnosis; THz spectroscopy and imaging.

Paper #9378 received 16 Oct 2025; revised manuscript received 31 Dec 2025; accepted for publication 31 Dec 2025; published online 10 Apr 2026. doi: 10.18287/JBPE26.12.020302.

1 Introduction

During the past decades, THz technology has been vigorously explored [1–4]. Nowadays, it has a potential in a number of applications, including the non-destructive testing [5], security task [6], label-free medical diagnostics of neoplasms [7, 8], cerebral ischemia, neurodegenerative diseases, traumatic injuries of the brain [9], diabetic foot syndrome [10], and even cancer therapy [11]. The majority of these applications involve measurements of the THz dielectric (optical) properties of an object. Despite the ubiquitous use of THz technologies, their translation into the aforementioned fields is hampered by the lack of THz endoscopes and methods to quantify the THz response of hard-to-access objects [7, 12]. In contrast to the visible–IR range with diverse fiber optics technologies, a lack of the THz fiber optics components and systems is evident, which leads to the nascent state of THz endoscopy [13, 14].

In this paper, recent attempts to address this challenging problem are considered. THz applications in medical diagnosis are overviewed, with an emphasis on neoplasms with the different nosologies and localizations [7]. Then, two distinct approaches of THz endoscopy are discussed [12]. The first uses the fiber-coupled THz PCAs to emit and detect THz waves in close proximity to a hard-to-access object [15, 16]. Such systems seem to be quite complex, cumbersome, and non-cost-efficient, which somewhat limits their practical utility. The second relies on the THz optical fibers / waveguides as key elements for delivering THz waves from an emitter to an object and then to detect the reflected THz signal. Although the THz optical fibers / waveguides still remain rare, expensive, and inefficient, recent developments in the THz fiber optics technologies pave the way to solve the demanding problem of THz endoscopy [12].

2 Results

We notice a few examples of THz waveguides and related endoscopic systems, which use the different material platforms, fabrication strategies, and guiding mechanisms, such as the reflection from walls in metal tubes [17], total internal reflection in step-index fibers [18], anti-resonant reflecting optical waveguiding

This paper was presented at the XI International Conference "Information Technology and Nanotechnology" (ITNT-2025), Samarkand, Uzbekistan, October 7 – 9, 2025.

(ARROW) [19] or photonic crystalline (PC) / Bragg waveguiding [20] in microstructured fibers, as well as plasmonic waveguiding [21].

Several THz fiber optics elements were developed by our research group relying on the EFG-grown sapphire shaped crystals [14]. A favorable combination of the unique physical and chemical properties of sapphire (high refractive index and low absorption in the THz range, high mechanical and radiation strength, chemical inertness, and biocompatibility) with the capabilities of the EFG technique to produce crystals of a delicate cross section directly from the Al_2O_3 melt, makes the EFG-grown sapphire shaped crystals an attractive material platform of THz fiber optics.

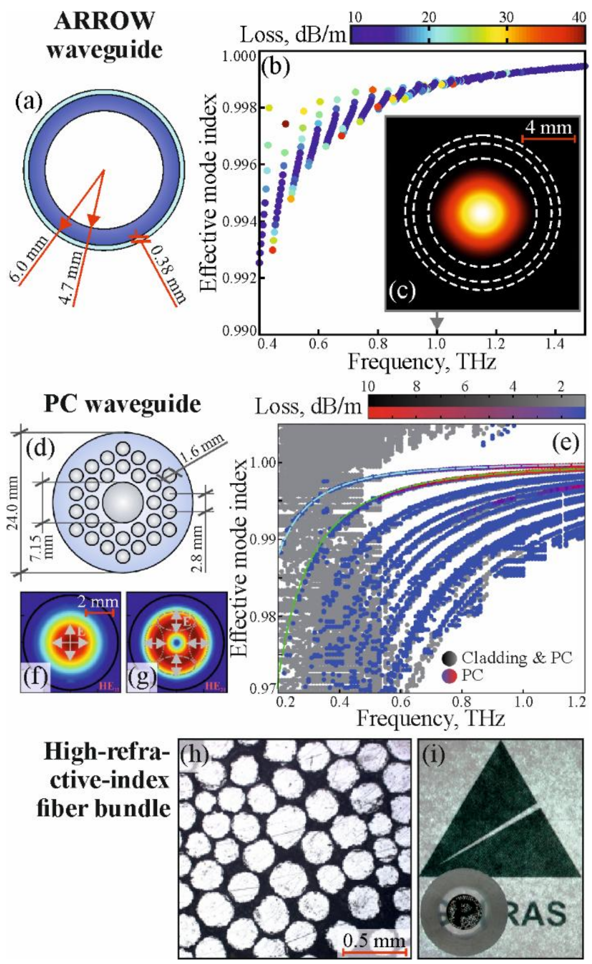

Fig. 1 A few examples of the EFG-grown THz fiber optics elements. (a–c) Scheme of the cross-section of the ARROW THz waveguide based on a PTFE-coated sapphire tube, along with the guiding properties (effective mode index and propagation loss) and intensity distribution (over the cross-section) for the fundamental mode in such waveguide. (d–g) Similar data set for the sapphire PC THz waveguide with two core-guided effective modes. (h),(i) Microscopy and photo of the THz optical fiber bundle formed by the sub-millimeter-diameter step-index sapphire fibers suspended in epoxy resin. Courtesy of K.I. Zaytsev.

In this way, the EFG technique was applied to produce:

- the hollow-core ARROW (Figs. 1 (a–c)) or PC (Figs. 1 (d–g)) waveguides for the THz-wave delivery and intrawaveguide sensing [22–25];
- the single step-index optical fibers for the THz scanning-probe near-field optical microscopy [26, 27];
- the optical fiber bundles for the superresolution THz imaging (Figs. 1 (h, i)) [28–30].

Most recently, the THz endoscope based on the hollow-core ARROW waveguide was developed by our group [31]. For this, the polytetrafluoroethylene (PTFE)-coated EFG-grown sapphire tube was used, as a key element, as shown in Fig. 2 (a). This system made it possible, for the first time, to quantify the THz optical properties of hard-to-access objects, such as biological tissues and internal organs. Our endoscope was attached to the in-house reflection-mode backward wave oscillator (BWO) spectrometer. The latter relies on the in-house continuous-wave BWO (the output frequency ranges from $\nu = 0.550$ to 0.715 THz, while the spectral linewidth is as narrow as $\sim 10^{-5}\nu$) [32, 33] and the in-house Golay cell (the THz-beam intensity detector) [34]. The outer end of the endoscope was closed by a $d = 1$-mm-thick c-cut (i.e. the optical axis is collinear to the sapphire c-axis) sapphire window, that serves both as a sample holder and a Fabry-Perot sensor of refractive index of an analyte.

In Figs. 2 (b–d), we show examples of the sapphire window reflectivity measured through the endoscope, when it is placed in contact with different test media, with a priori known THz refractive indices: air, liquid water, and propylene glycol (PG). Changes in the parameters of the Farby-Perot minimum in the reflectivity spectra are evident. Their analysis makes it possible to quantify the THz complex refractive index of an analyte [31]. For this, let us define the complex refractive index of sapphire

$$\tilde{n}_{Al_2O_3} = n_{Al_2O_3} - in''_{Al_2O_3} = n_{Al_2O_3} - i\frac{c_0}{4\pi\nu}\alpha_{Al_2O_3}, \quad (1)$$

$n_{Al_2O_3}$ and $\alpha_{Al_2O_3}$ are the real refractive index and power absorption coefficient (both – for the ordinary ray) [35], $c_0 = 3 \times 10^8$ m/s is the speed of light in free space), guided mode (Fig. 1(b))

$$\tilde{n}_{eff} = n_{eff} - in''_{eff} = n_{eff} - i\frac{c_0}{4\pi\nu}\alpha_{eff} \cong 1, \quad (2)$$

and analyte

$$\tilde{n} = n - in'' = n - i\frac{c_0}{4\pi\nu}\alpha. \quad (3)$$

Then, the magnitude and position of the local Fabry-Perot minimum in the reflectivity curves (Figs. 2 (b–d)) take the forms [36]:

$$R_{min} = \left|\frac{\tilde{r}_{eff-Al_2O_3} - \tilde{r}_{Al_2O_3-analyte}}{1-\tilde{r}_{eff-Al_2O_3}\tilde{r}_{Al_2O_3-analyte}}\right|^2, \quad (4)$$

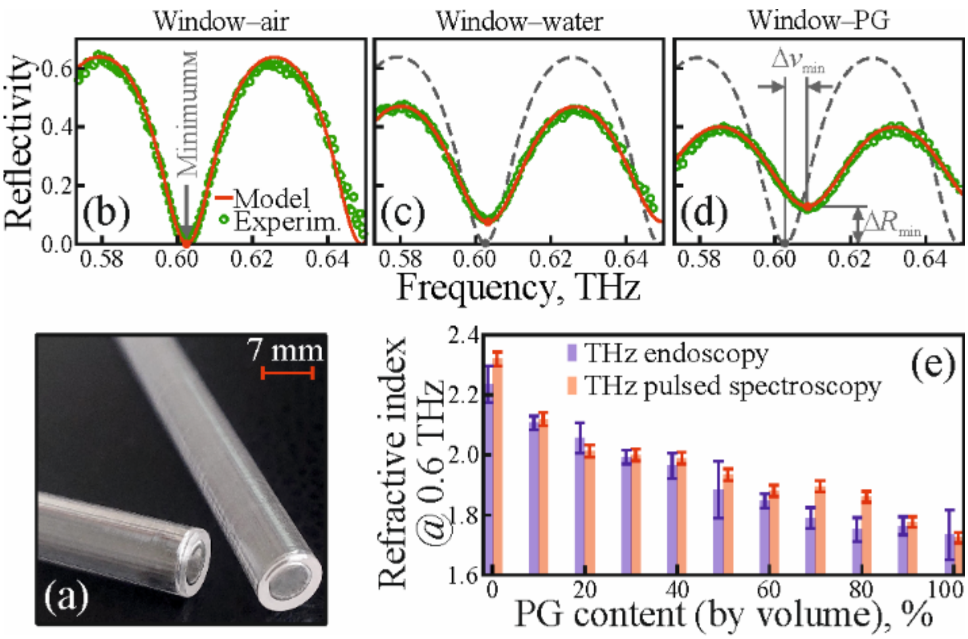

Fig. 2 THz endoscopy of hard-to-access test objects using the ARROW THz waveguide made of the EFG-grown sapphire tube coated by PTFE. (a) A photo of the THz endoscopes, with the output ends closed by monolithic (as-grown) d = 1-mm-thick sapphire window. (b–d) Fabry-Perot resonances (minima) observed in the reflectivity of the sapphire window with a free space, liquid water and PG, respectively, placed at its shadow side. (e) Endoscopic determination of the refractive index (at 0.6 THz) of the liquid analytes (namely, the PG aqueous solutions of the different volume fractions) as compared to the reference transmission-mode measurements by the THz pulsed spectrometer. Courtesy of K.I. Zaytsev.

$$\nu_{min} = \frac{c_0}{4 d n_{Al_2O_3}} \left(\frac{\varphi}{\pi} + (2m+1) \right), \quad (5)$$

where $m = 0, \pm 1, \pm 2, \ldots$ is an integer, $\tilde{r}_{eff-Al_2O_3}$ and $\tilde{r}_{Al_2O_3-sample}$ are the Fresnel amplitude reflection coefficients (at the normal incidence) for the "waveguide core–sapphire" and "sapphire–analyte" interfaces defined as:

$$\tilde{r}_{eff-Al_2O_3} = \frac{\tilde{n}_{eff} - \tilde{n}_{Al_2O_3}}{\tilde{n}_{eff} + \tilde{n}_{AAl_2O_3}}, \quad (6)$$

$$\tilde{r}_{Al_2O_3-analyte} = \frac{\tilde{n}_{AAl_2O_3} - \tilde{n}}{\tilde{n}_{Al_2O_3} + \tilde{n}}, \quad (7)$$

φ is the phase shift at the "window–analyte" interface:

$$\varphi = arctan\left[\frac{2 n_{Al_2O_3} n''}{n^2_{Al_2O_3} - n^2 - n''^2}\right]. \quad (8)$$

Using the developed THz endoscope and the inferred equations, in Fig. 2 (e), we characterize the refractive indices of the PG aqueous solutions with different volume fractions. One observed good agreement between our THz endoscopic measurements and those performed by the in-house reflection-mode THz pulsed spectrometer [37–39]. This highlights capability of our THz endoscope to measure the THz dielectric response of hard-to-access objects at the distances of about ~10 cm, and even larger.

The developed THz endoscope and the related data processing routine pave the way for THz technology application in different demanding branches of science and technology, which require the THz-wave delivery to a hard-to-access object, including the THz medical diagnosis of internal tissues and organs. Moreover, the advanced chemical inertness and thermal strength of the endoscope materials (i.e., the sapphire and PTFE), make it possible to apply thus developed system for sensing in harsh environments. This feature additionally broadens the range of the THz endoscopy applications.

Nevertheless, to objectively uncover the strengths and weaknesses of the developed THz endoscopy hardware and software, additional studies of some real-world objects (such as healthy and pathologically-altered tissues, chemical and pharmaceutical analytes, materials, etc.) are in order. Reduction of the outer diameter of such a THz endoscope down to the realistic values of ~3–4 mm is also preferable for its applications in minimally-invasive medical procedures. We postpone all these studies and upgrades to our future research work.

3 Conclusion

In this paper, we focused on recent attempts to mitigate the problem of THz endoscopy of hard-to-access tissues and internal organs. The two existing principles of THz endoscopy were considered:

- The first uses the fiber-coupled THz PCAs for the THz generation and detection in close proximity to an object, while quartz optical fibers are used to deliver the laser pump and probe beams to these PCAs.
- The second relies on the THz optical fibers / waveguides to deliver THz waves to an object and

then to detect the reflected and back-propagated THz signal.

The most recent developments in the area of THz fiber optics are discussed. They pave the way to solve the challenging problem of THz endoscopy. Among them: the THz fibers, fiber bundles, waveguides, and endoscopes developed by our group relying on the EFG-grown sapphire shaped crystals.

Disclosures

All authors declare that there is no conflict of interest in this paper.

Acknowledgements

This work is supported by the Russian Science Foundation, Project # 22–79–10099.

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