Fabrication and characterization of biotissue-mimicking phantoms in the THz frequency range

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Abstract. The study revealed the most promising candidates for phantoms mimicking different biological tissues in the terahertz frequency range. Closest to biological tissues in terms of the refractive index appeared to be gelatin-based gels; in terms of the absorption coefficient they were agar-based gels. Gelatin is more stable in time, but requires special storage conditions to limit water evaporation. The dense structure of the agar-based phantom allows its use without mold and risk of damage. However, agar is a nutrient medium for bacteria and its parameters degrade even when the phantom form and water content are retained. Use of liquid suspensions of lecithin and milk powder are found to be extremely limited.

1. Introduction

A number of applications demand for stable objects with preset properties. New biomedical devices require tests to reveal their performance and, later on, periodic calibration to maintain the properties over time at the proper level. Familiarization of young researchers from biomedical engineering field with functioning principles of biological tissues and organs finds obstacles in many technical universities and laboratories due to lack of equipment and facilities necessary for working with biological objects such as animal or human cultured cells [1], blood [2] etc [3]. In particular, specific requirements are set for educational labs, where students are trained. In case of optics and photonics, test objects termed *phantoms* should possess optical properties of biological tissues and be stable in time.

A phantom is a biotissue-mimicking material molded with a specific shape having a range of real-tissue properties, such as elasticity, refractive index, scattering and absorption coefficients, stability over time etc. For most types of modern medical diagnostics a variety of phantoms are commercially available [4-6]. However, only the first steps are performed in this direction at the moment for terahertz (THz) frequency range, mainly in a form of a catalog of parameters of various biological and organic gels. This work shows characteristics of various biological tissues at the THz spectral range and suggests the most promising candidates for mimicking them.

2. Materials and methods

2.1 Terahertz time-domain spectrometer

Study on phantoms and biological tissues was performed by time-domain spectroscopy using a system developed in ITMO University [7-9]. Broadband pulsed terahertz radiation was generated by a semiconductor undoped crystal of indium arsenide upon its irradiation with femtosecond pulses of KYW:Yb laser (wavelength of 1040 nm, duration of 120 fs, pulse frequency of 70 MHz, power of 1.2 W). Characteristics of the emitted THz radiation are the following: the frequency ranges from 0.1 to 1.8 THz, average power of 0.3 μW and pulse duration of 2.7 ps [9,10]. Most of the power was spread within the 0.1 to 0.6 THz frequency range. In the frequency range from 1.0 to 1.8 THz, the signal did not exceed 1% of the maximum value. The sample was fixed perpendicularly to the optical axis in the focal plane using a two-axis motorized translation stage. Electro-optical detection was carried out using a quarter-wave plate, a Wollaston prism, a balanced photodetector and a lock-in amplifier. Filtered and amplified signals were transmitted to a computer via a digital voltmeter. Spectral resolution during measurements was about 7 GHz in the transmission mode and 15 GHz in the reflection mode. System control was performed by an in-house written code in LabVIEW software.

Biological samples and phantoms were placed at the bottom of a plastic one-well plate. The samples were covered with a silicon window (thickness is 1.04 mm, refractive index of 3.5). Measurements were performed in the reflection mode. Each point of the scanned pulse was averaged 100 times.

2.2 Preparation of biological tissue

Tissue samples were taken from different animals, *post mortem*. A blood vessel was cut out from a fresh sheep heart (N_{exp} = 5). The sample was dried and straightened. An adipose tissue was cut out of a cow kidney (N_{exp} = 10). Peripheral blood was drawn from tails of white laboratory mice. Blood was not centrifuged (N_{exp} = 4). Pig eye cornea was investigated (N_{exp} = 3). A human skin sample was taken from a front wall of a breast of a fifty-two-year-old woman.

2.3 Preparation of phantoms

Gelatin is a partially hydrolyzed collagen. It is a resultant product of processing or denature of animal connective tissue. Collagen comprises about ~20% of all proteins of the human body, and therefore gelatin was chosen as the best study object. In order to create a phantom, 10 g gelatin was first soaked in cold water (15 °C) to form a gelled granular paste at concentrations of 1:25, 10:125 and 100:625. After that, the temperature was elevated to 60 °C, with constant stirring, until formation of a pale-yellow liquid poured into a mold and cooled for 12 hours. The mold was aligned to ensure parallelism of upper and lower phantom surfaces. Its melting point is about 35 °C, so the sample was stored in the refrigerator between the experiments.

Agar is a mixture of polysaccharides of agarose and agaropectin extracted from red and brown algae growing on the costs of the Black Sea, the White Sea and the Pacific Ocean, which forms a dense jelly substance in water solutions. Agar is insoluble in cold water. 5 g powder was soaked in the ratio of 5:167, 5:50 and 5:30 for one hour. The resulting mixture was heated to a boiling point, since agar is fully dissolved in water at the temperature of 95-100 °C. The hot solution is transparent and partially viscous. Upon cooling to 35-40 °C it becomes a clear strong heat-reversible gel. After that the solution was cast into a mold, with an adjusted level. The viscous mixture thickened within a few seconds, but for full curing the mold was placed into a cooling chamber at least for one hour. When pouring, the thickening liquid was stirred to avoid appearance of bubbles. The melting point of such phantom is above 75 °C, so the phantom is not necessarily be stored in the refrigerator.

For the preparation of liquid phantoms, two dry powders were used: lecithin (phospholipid) and powdered milk. 50 mg powder lecithin or milk powder was stirred in water in 1:10 ratio. Such phantom is very durable because of quickly water evaporation from the surface.

3. Results and Discussion

Optical characteristics of five different biological tissues within a 0.3-1.0 THz frequency range were retrieved. Phantoms were created with the parameters closest to biotissues (Figs. 1-7). The closest in terms of the refractive index were gelatin gels (4% for skin and cornea, 8% for blood and 16% for a blood vessel). The closest in terms of absorption coefficient were agar gels (10% for skin and a blood vessel) and gelatin gels (16% for blood).

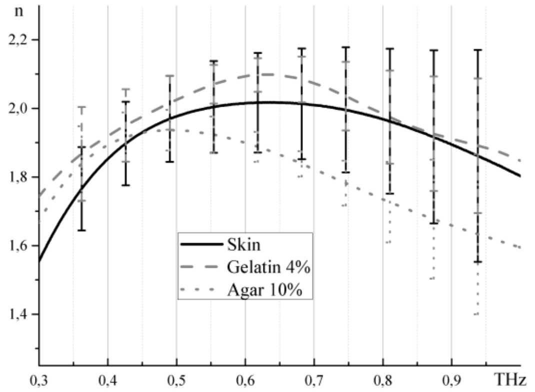

Figure 1. Dispersion of the refractive index of skin, gelatin 4% and agar 10%.

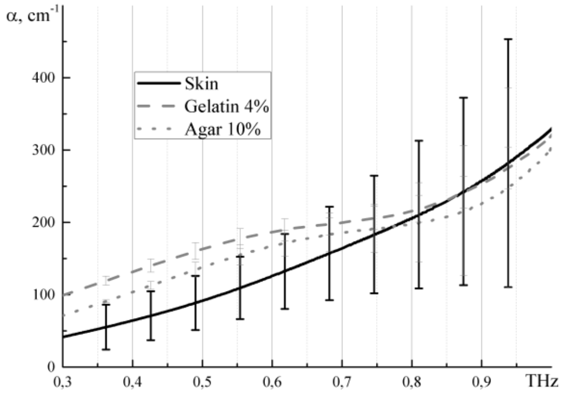

Figure 2. Dispersion of the absorption coefficient of skin, gelatin 4% and agar 10%.

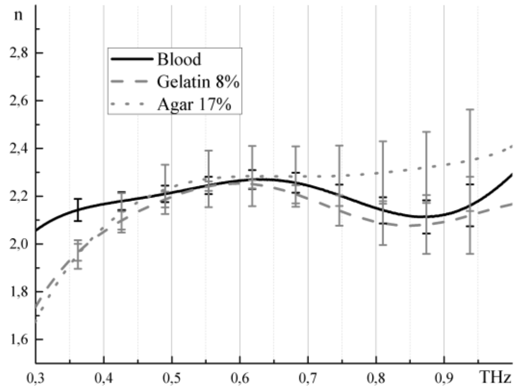

Figure 3. Dispersion of the refractive index of blood, gelatin 8% and agar 17%.

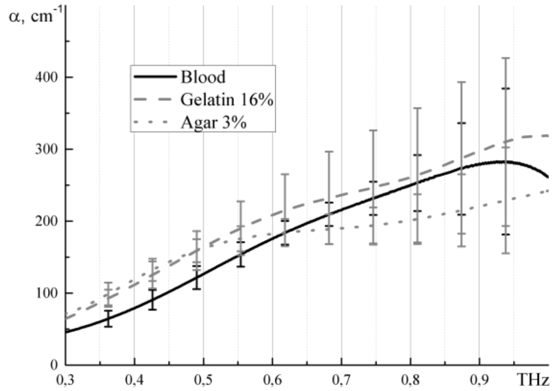

Figure 4. Dispersion of the absorption coefficient of blood, gelatin 16% and agar 3%.

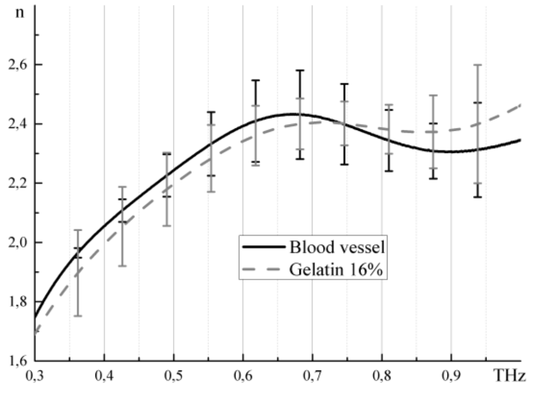

Figure 5. Dispersion of the refractive index of a blood vessel and gelatin 16%.

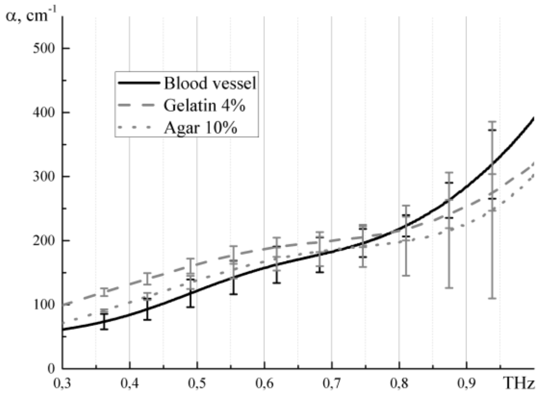

Figure 6. Dispersion of the absorption coefficient of a blood vessel, gelatin 4% , agar 10%.

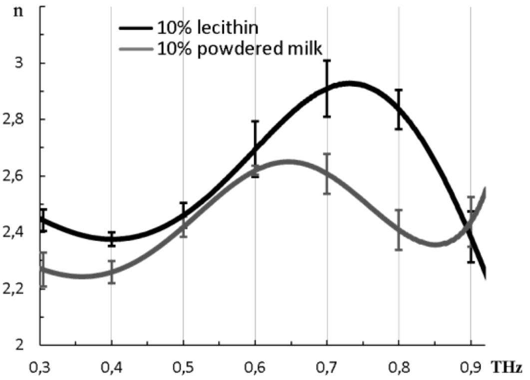

Figure 7. Dispersion of the refractive index of lecithin 10% and powdered milk 10%.

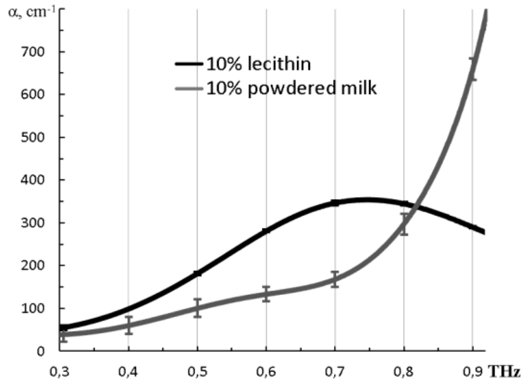

Figure 8. Dispersion of the absorption coefficient of lecithin 10% and powdered milk 10%.

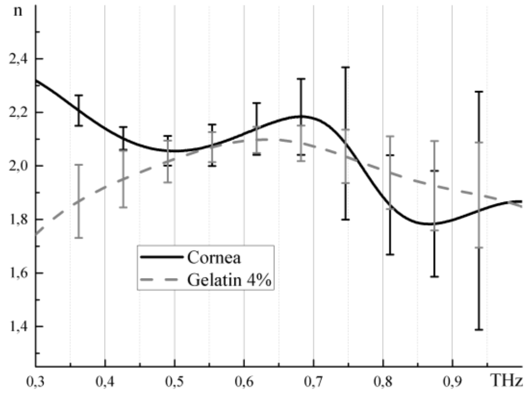

Figure 9. Dispersion of the refractive index of cornea and gelatin 4%.

4. Conclusion

The optimal phantoms for five types of biological tissues in the THz frequency range were identified during these researches. The gelatin gels were the closest in terms of the refractive index, agar gels were the closest in terms of the absorption coefficient. The gelatin gel is the optimal composite with density similar to many tissues; the cheapest and easiest to prepare. Its jelly-like structure provides a good optical contact with the substrate but it is very fragile and can be damaged during the measurement process. Gelatin is more stable in time, but it requires special handling to limit water evaporation. The dense structure of the agar phantom allows using it without mold and risk of damage. However, agar is a nutrient medium for bacteria, and its parameters degrade rapidly even with retained shape and water content. Use of aqueous suspensions of milk powder lecithin is found to be extremely limited.

Acknowledgments

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