

Terahertz microfluidic biosensor based on metamaterial absorber

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Terahertz living cell analysis is a hot spot in the field of spectral research, and its main difficulty lies in how to effectively avoid the interference of water and carry out sensitive analysis and detection of samples in liquid phase environment. In order to reduce the strong absorption of terahertz by water when testing solution samples, and improve the sensitivity of the sensor. In this paper, a terahertz microfluidic biosensor based on metamaterial absorber is designed. The sensor chip integrates metamaterial absorber and microfluidic channel. There are two perfect absorption peaks in 0.69 THz and 0.95 THz in THz band, and the refractive index sensitivity can reach 305 GHz/RIU. The experimental results show that the proposed dual-band terahertz sensors are insensitive to polarization and wide incident angle. In addition, when the samples with different refractive index pass through the microfluidic channel, the high and low resonance peaks show different red shifts, and then the material detection is realized by analyzing the red shift difference between the high and low resonance peaks of different substances. Therefore, the metamaterial terahertz microfluidic biosensor has a good application potential in the field of unlabeled trace matter detection, and can provide new ideas for terahertz biomedical research.

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1. Introduction

In recent years, spectral technology is considered to be one of the most important methods in the field of biomolecule sensing, and the use of spectroscopy to achieve rapid, label-free and sensitive detection of biological macromolecules has been widely studied. The unique advantages of terahertz (THz) spectroscopy in the field of biomedical sensing have attracted the attention of many researchers [1]. Metamaterial terahertz biosensor is a sensitive unlabeled optical sensor by transforming the change of dielectric constant of the test sample into optical signal. As a new detection method in biomedical field, metamaterial terahertz sensor has many unique advantages, such as (1) high sensitivity; (2) trace substance; (3) fast response and rapid detection; (4) simple operation flow. In recent years, with the development of micro-nano processing technology, the cost of making metamaterial terahertz sensors is more acceptable. At the same time, the metamaterial terahertz sensor has become a research hotspot in the terahertz field because of its excellent performance. At present, it has been used in the quantification of macromolecular compounds [2-4], cell viability evaluation [5], virus recognition [6] and so on. Because of the strong absorption of water in the THz domain, the above studies are measured indirectly by deposition method, but most biological samples can maintain biological activity only in liquid environment, so

this method cannot accurately characterize the information of biological samples. Microfluidic chip can be used in terahertz field to overcome the absorption of water because of its low cost, limited sample size and rapid detection [7]. At present, in the THz band, there have been studies on the use of microfluidic chips to sense high absorption solution [8-9], but due to the lack of measures to improve the sensitivity, its sensitivity is still limited.

Microfluidic technology can realize the detection of micron or even nanometer substance, which has been widely used in the field of sensing [10-11]. The combination of metamaterial absorber and microfluidic technology can provide a new idea for the design of terahertz sensor. When the electromagnetic wave is incident, the Fabry-Perot structure of the metamaterial absorber binds the energy of the incident wave in the cavity of the absorber [12], and the substance in the Microfluidic channel is used as the dielectric layer of the metamaterial absorber, which coincides with the reflection cavity, which significantly enhances the local electromagnetic field and effectively improves the sensitivity of the sensor. In addition, the Microfluidic channel controls the solution volume to the order of micron, which effectively reduces the absorption of terahertz wave by water, which is helpful to realize the highly sensitive detection of solution samples. Terahertz sensors integrated with metamaterial absorbers and microfluidic have great potential in glucose detection [13],

cancer diagnosis [14], biomedicine [15] and so on.

Based on this, a high sensitivity terahertz microfluidic biosensor based on metamaterial absorber is designed by combining microfluidic technology. The sensor can produce two perfect absorption peaks with an absorptivity of 99% in the 0.2-1.5 THz band, with a sensitivity of 305 GHz/RIU and a Q value of 43.9. In addition, because the unit structure of terahertz microfluidic biosensor is symmetrical, it is insensitive to polarization and wide incident angle, and can maintain good sensing performance in a wide range.

2. Structural design

Fig. 1(a) shows the unit structure of the terahertz microfluidic biosensor with a metamaterial absorber. The sensor is composed of five layers, which are dielectric

layer, metal microstructure, microfluidic channel, metal reflector and substrate from top to bottom. Among them, the dielectric layer is made of quartz with a dielectric constant of $3.75+i0.015$ and a thickness of $4\ \mu\text{m}$. Both the metal layer and the metal reflector use gold with a conductivity of $4.52\times 10^7\ \text{S/m}$ and a thickness of $0.1\ \mu\text{m}$. The substrate is selected as the silicon material which will not affect the performance of the sensor, its dielectric constant is 11.9 and the thickness is $50\ \mu\text{m}$. The unit structure period $l_1=120\ \mu\text{m}$. The microfluidic channel is located between the metal reflector and the metal microstructure with a height of $h_3 = 5\ \mu\text{m}$. The metal microstructure of the sensor consists of a square metal notch ring and a circular metal notch ring (as shown in Fig. 1(b)), and the optimized geometric parameters are shown in Table 1.

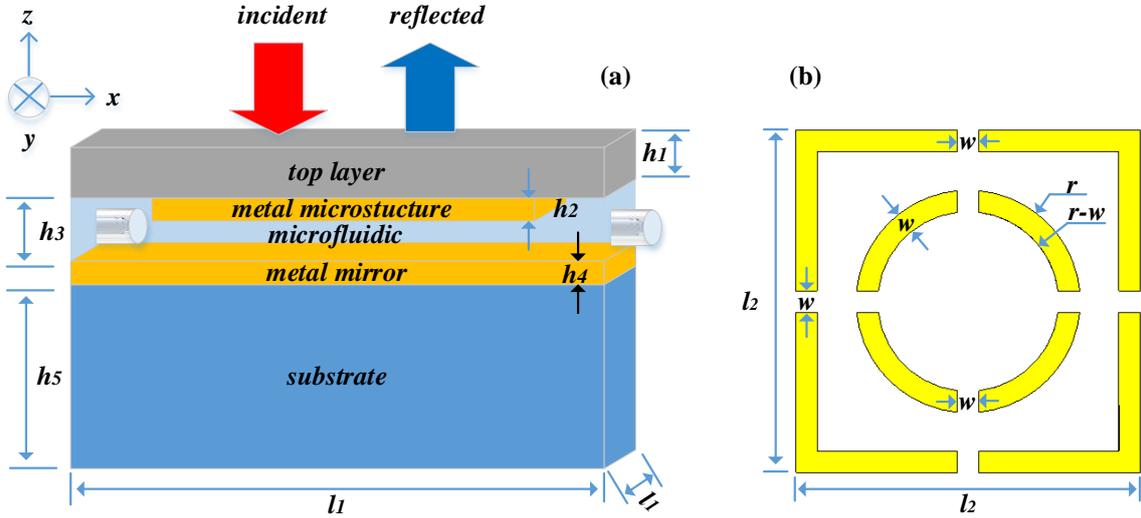


Fig. 1. Schematic diagram of unit structure of terahertz sensor. (a) side view of unit structure; (b) metal microstructure unit of sensor (color online)

Table 1. Geometric parameters of structural unit of terahertz microfluidic biosensor

Parameters	l_1	l_2	r	w	h_1	h_2	h_3	h_4	h_5
Value/ μm	120	100	65	5	4	0.1	5	0.1	50

3. Results and analysis

3.1. Sensing performance index

The quality factor Q is used to characterize the optical resonance properties of the sensor. The larger the Q is, the

smaller the loss of the resonance system is, the narrower the resonance peak is, and the easier it is to distinguish the change of the measured spectrum [16]. The Q of the sensor can be expressed as $Q = f_0 / X_{FWHM}$. In the formula,

f_0 is the resonant frequency and the X_{FWHM} is full width of the half peak. Refractive index sensitivity S is an important index to measure the performance of the sensor. The larger the refractive index sensitivity S is, the easier it is to reflect the small change of dielectric properties around the sensor in the spectrum, which can be expressed as $S = \Delta f / \Delta n$. In the formula, Δf is the change of resonant frequency and Δn is the change of refractive

index, in units of refractive index unit (RIU). The quality factor (FOM) can characterize the overall performance of the sensor and analyze the performance of the sensor in different frequency bands more reasonably. The higher the value of FOM is, the better the overall performance of the sensor is. The calculation formula of FOM can be expressed as $X_{FOM} = S / X_{FWHM}$.

3.2. Analysis of sensing performance

The absorptivity of the sensor can be expressed as

$$A(\omega) = 1 - R(\omega) - T(\omega) = 1 - |S_{11}|^2 - |S_{21}|^2, \text{ where } \omega \text{ is the}$$

frequency, $R(\omega)$ is the reflectivity, $T(\omega)$ is the transmittance, S_{11} is the reflection coefficient and S_{21}

is the transmission coefficient. The thickness of the metal reflector of the Hertz sensor designed in this paper is 0.1 μm , which is much larger than the skin depth of the terahertz wave in the metal. The terahertz wave cannot pass through the metal reflector, and the transmittance is almost 0, that is, $T(\omega) = 0$. Fig. 2(a) shows the reflection and absorption spectrum of the designed terahertz sensor when there is no sample in the microfluidic channel. It can be found that the sensor produces absorption peaks with an absorption rate of 99.9% at 0.69THz (low frequency) and 0.95 THz (high frequency). According to the quality factor formula, the Q values of the sensor at low frequency and high frequency are 31.8 and 43.9, respectively. The unit structure of the terahertz sensor designed in this paper is symmetrical and has polarization insensitivity. Fig. 2(b) shows the absorption spectra of terahertz sensors under TE and TM polarization electromagnetic waves. It can be found that the absorption spectra of the two polarization modes are highly consistent, which indicates that the polarization direction of electromagnetic waves has no effect on the detection results of the sensor.

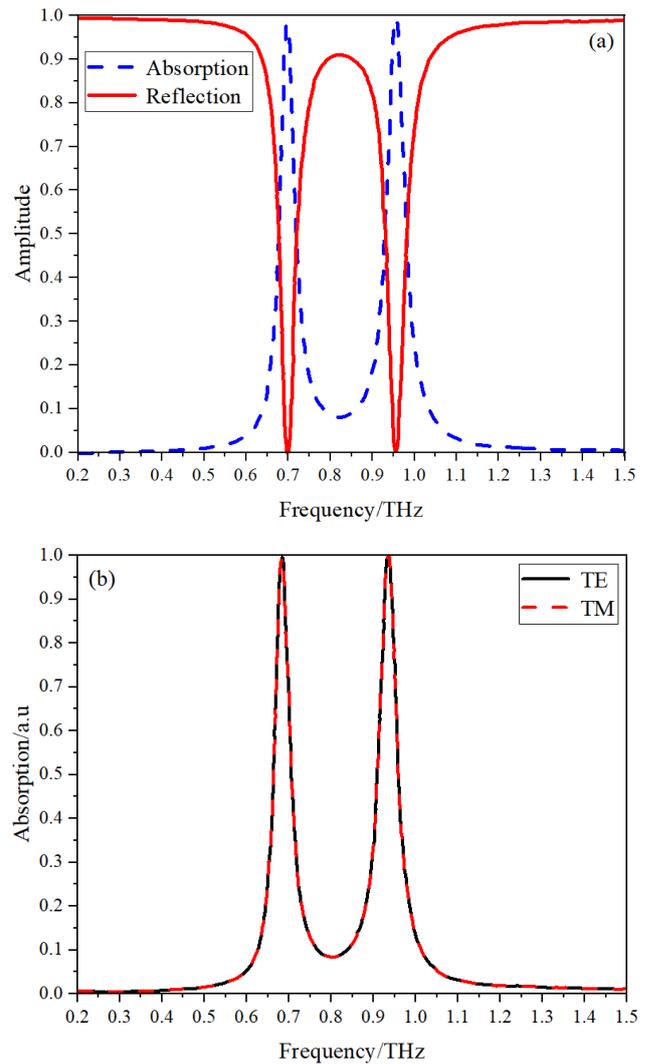


Fig. 2. Terahertz spectrum of sensor without sample in microfluidic channel. (a) absorption and reflection spectrum; (b) absorption spectrum of sensors under polarized electromagnetic waves of TE and TM

Studies have shown that the refractive index of common medical samples such as DNA is 1.41.6 [17], the refractive index of blood of healthy people is 1.35 [18], and the refractive index of normal basal cells with a concentration of 40%, 60%, is 1.36 [19]. In order to apply the sensor designed in this paper to the detection of common biomedical samples, the refractive index n of the sample set in this paper varies from 1.0 to 1.6 (step size 0.2). When the sample passes through the microfluidic channel, the change of the refractive index of the sample leads to a change in the dielectric environment around the metamaterial, and the metamaterial absorber acutely converts this change into the change of terahertz wave signal. It is reflected in the change of the resonance curve in the spectrum. Fig. 3(a) the corresponding absorption spectrum of different refractive index sample in the

microfluidic channel of the terahertz sensor. It can be found that when the refractive index n of the sample increases from 1.0 step 0.2 to 1.6, the resonance peak of the sensor has an obvious red shift (to low frequency). This shows that the sensor can be used for the detection of biomedical samples. Fig. 3(b) shows the relationship between the frequency shift of the terahertz sensor and the change of refractive index. It can be found that the

resonant frequency shift of the sensor increases gradually when the sample refractive index n changes from 1.0 to 1.6 (step size is 0.1), and basically maintains a linear relationship with the refractive index. The linear fitting results show that the sensitivity of the sensor at low frequency resonance point and high frequency resonance point is 220 GHz/RIU and 305 GHz/RIU respectively.

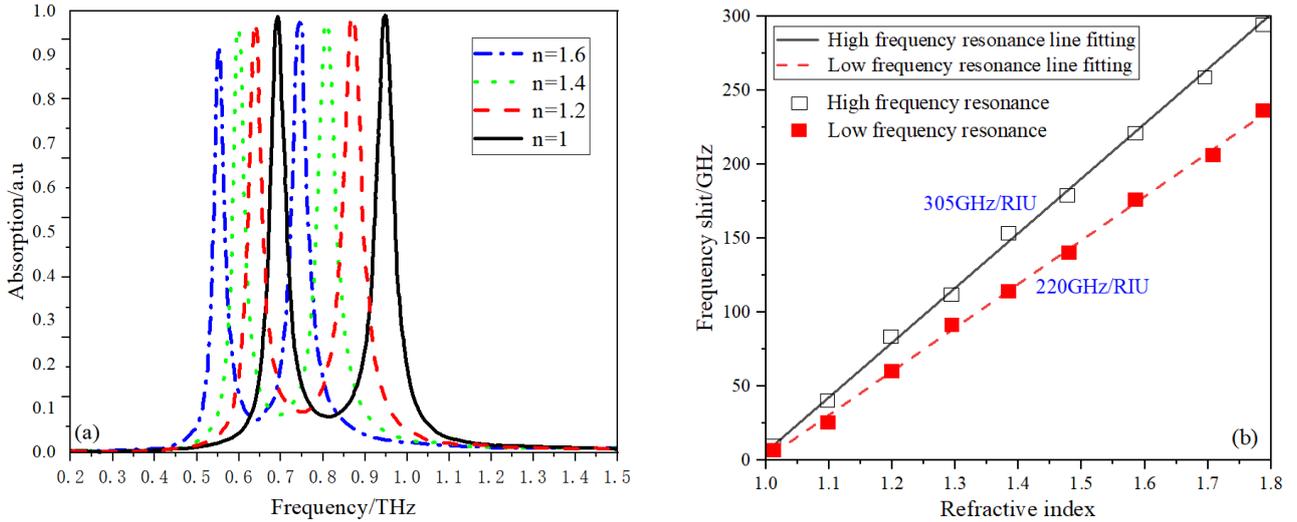


Fig. 3. Refractive index detection characteristics of sensor. (a) absorbers for samples with different refractive index; (b) linear fitting and simulation of frequency shift of high and low resonant (color online)

Table 2. Comparison between the proposed sensor and the sensor in the reference

Reference	Resonance frequency	sensitivity	Absorptivity
Ref.[20]	0.79THz	0.379 THz/RIU	98.8%
Ref.[21]	1.28 THz	0.51 THz/RIU	99.5%
Ref.[22]	0.76THz, 2.06THz	0.47THz/RIU, 72GHz/RIU	99.8%
Ref.[23]	0.64THz, 0.88THz	206 THz/RIU, 300 THz/RIU	99.9%
Proposed	0.69THz, 0.95THz	220 THz/RIU, 305 THz/RIU	99.9%

Table 2 shows the performance comparison between the terahertz microfluidic biosensor proposed in this paper and the sensor in other references. It can be found that the terahertz sensor designed in this scheme has the characteristics of high absorptivity and high sensitivity, and has potential application value in the field of sensor detection.

3.3. Stability analysis

In order to avoid the error caused by optical polarization in practical application, the unit structure of the terahertz microfluidic biosensor designed in this paper is symmetrical and polarization insensitive. Therefore, this

paper only analyzes the influence of incident angle on the performance of terahertz microfluidic biosensor in TE mode. Fig. 4 shows the shift of the high and low resonant frequency of the terahertz microfluidic biosensor with the incident angle. When the refractive index n of the sample in the microfluidic channel changes from 1 to 1.6, and the incident angle θ is less than 60° , the absorptivity of the low frequency absorption peak of the sensor is more than 95%, the high frequency absorptivity is more than 99%, and the resonant frequency does not shift significantly. This shows that the designed terahertz sensor is insensitive to a wide incident angle of $0-60^\circ$.

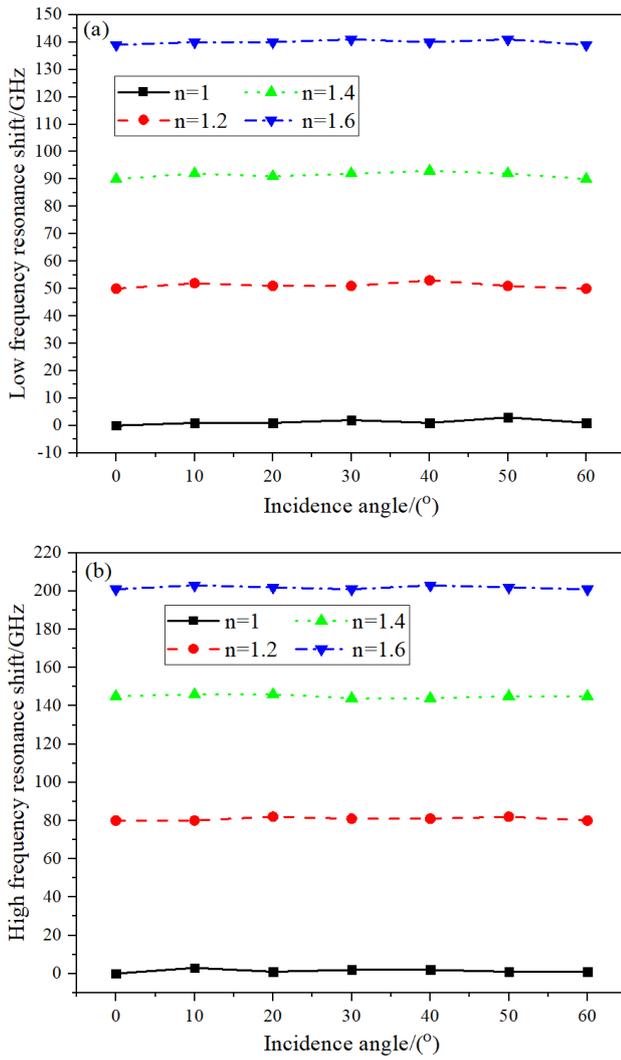


Fig. 4. Variation of absorptivity and frequency shift of sensor with incident angle. (a) low frequency resonance; (b) high frequency resonance (color online)

When the incident terahertz wave enters the multi-layer structure sensor, part of the terahertz wave will be reflected many times between the metal microstructure layer and the metal reflector, and this part of the terahertz wave will be bound in the microfluidic channel. By changing the height of the microfluidic channel (h_3), the equivalent impedance of the sensor can be changed to match the impedance of the free space, so as to enhance the absorption of terahertz wave. In order to find the best impedance matching, the effect of microfluidic channel height on the absorptivity and Q value of the absorption peak of the sensor is analyzed (other parameters remain unchanged). Fig. 5 shows the relationship between the microfluidic channel height and the sensor absorption peak and Q value. As can be seen from the figure, when the height of the microfluidic channel is 5 μm , the sensor and the free space can form the best impedance matching effect, and the absorptivity and Q value of the low

frequency and high frequency resonance peaks of the sensor reach the maximum.

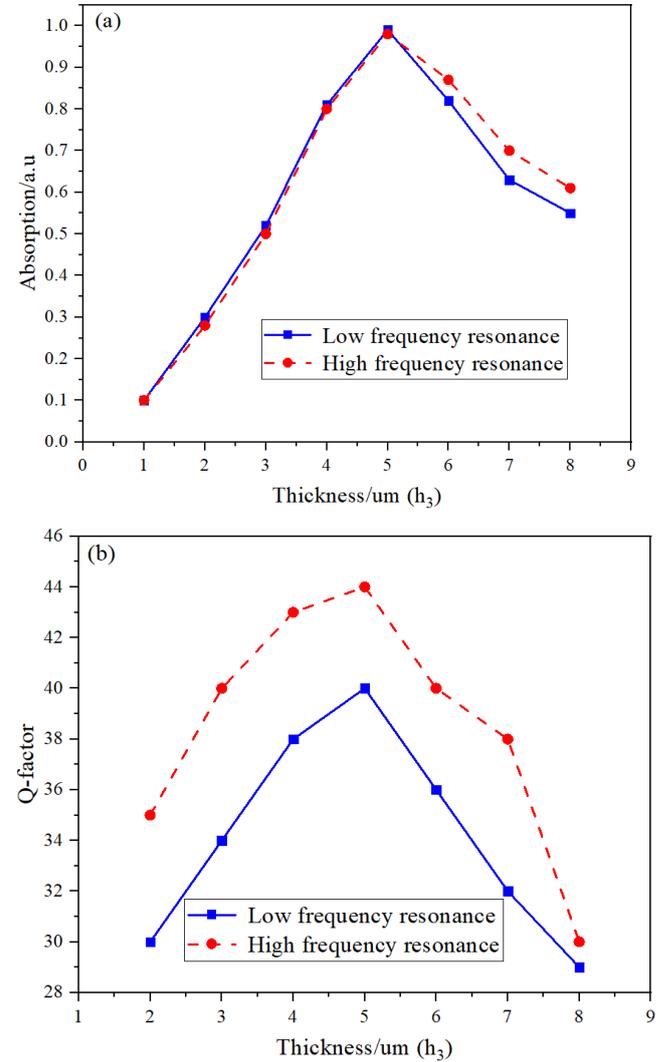


Fig. 5. Variation of absorptivity and Q value of low-frequency and high-frequency resonant points of sensors with the height of microfluidic channel (color online)

In order to further analyze the influence of the dielectric layer on the sensitivity of the terahertz sensor, Fig. 6 shows the relationship between the dielectric constant and the thickness of the dielectric layer and the sensitivity of the sensor's high and low absorption peaks (the height of the microfluidic channel is fixed at 5 μm). When the thickness of the dielectric layer is fixed (4 μm in this paper) and the dielectric constant of the dielectric layer increases from 1.84 to 11.9, the sensitivity of the low frequency resonance peak decreases from 220 GHz/RIU to 180 GHz/RIU, and the sensitivity of the high frequency absorption peak decreases from 305 GHz/RIU to 255 GHz/RIU. When the dielectric constant of the dielectric layer is fixed (3.75 in this paper) and the thickness of the dielectric layer increases from 4 μm to 24 μm , the

sensitivity of the sensor decreases gradually. It is not difficult to find that the increase of the dielectric constant and thickness of the dielectric layer will lead to the decrease of the frequency offset and sensitivity of the high and low frequency absorption peaks. However, the sensitivity of the sensor will not decrease infinitely with the increase of the thickness of the dielectric layer. When the thickness of the dielectric layer increases from 24 μm to 94 μm , the sensitivity of the sensor remains unchanged, and the sensitivities of low frequency and high frequency absorption peaks are 255 GHz/RIU and 180 GHz/RIU, respectively. At this time, because the electromagnetic field excited by the sensor has been basically covered by the dielectric layer, increasing the thickness of the dielectric layer will not affect the equivalent capacitance of the sensor, and the sensitivity tends to be saturated.

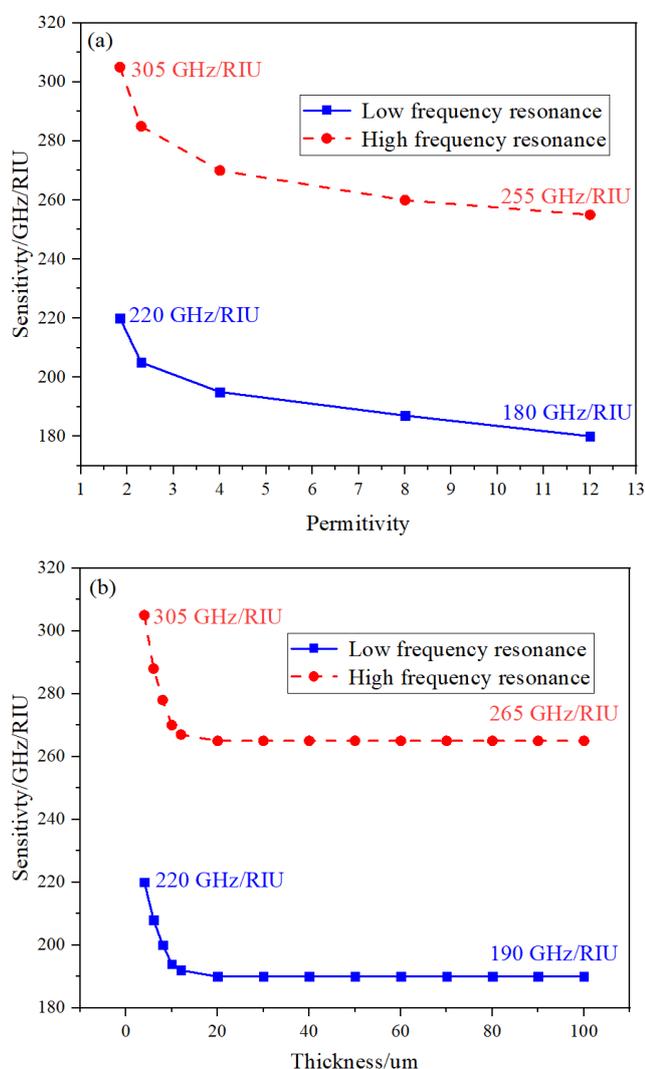


Fig. 6. Effect of dielectric constant and thickness of dielectric layer on the sensitivity of high and low absorption peaks of the sensor (color online)

4. Conclusion

In order to reduce the strong absorption of water to terahertz and improve the sensitivity of the sensor, a terahertz microfluidic biosensor is proposed on the basis of metamaterial absorber and introducing microfluidic channel. The sensor chip integrates a metamaterial absorber and a microfluidic channel, which can produce two perfect absorption peaks with an absorption rate of 99.9% in the 0.2-1.5 THz band, and the refractive index sensitivity can reach 305 GHz/RIU. In addition, the unit structure of the designed terahertz sensor is symmetrical, which is insensitive to polarization and wide incident angle, and shows good sensing performance in the range of incident angle from 0 ° to 60 °. The designed terahertz microfluidic biosensor has a broad application prospect in the field of biomedicine.

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References

- [1] Xiang Yang, Xiang Zhao, Ke Yang, Yueping Liu, Yu Liu, Weiling Fu, Yang Luo, Trends in Biotechnology **34**(10), 810 (2016).
- [2] W. Xu, L. Xie, J. Zhu, ACS Photonics **3**, 2308 (2016).
- [3] Oh-e. Masahito, Deng-Yun Zheng, Scientific Reports **12**, 5482 (2022).
- [4] Xiaoyan Liu, Min Qian, Food Chemistry **349**, 129131 (2021).
- [5] Yu Liu, Mingjie Tang, Liangping Xia, Wenjing Yu, Jia Peng, Yang Zhang, Marc Lamy de la Chapelle, Ke Yang, Hong-Liang Cui, Weiling Fu, RSC Adv. **7**, 53963 (2017).
- [6] Bogyu Kim, Young-Uk Jeon, Joon Hyun Kang, Scientific Reports **12**, 5363 (2022).

- [7] Kazunori Serita, Hironaru Murakami, Iwao Kawayama, Masayoshi Tonouchi, *Photonics* **6**(1), 12 (2019).
- [8] Mingkun Zhang, Zhongbo Yang, Mingjie Tang, Deqiang Wang, Huabin Wang, Shihan Yan, Dongshan Wei, Hong-Liang Cui, *Sensors* **19**(3), 534 (2019).
- [9] Xiang Zhao, Mingkun Zhang, Dongshan Wei, Yunxia Wang, Shihan Yan, Mengwan Liu, Xiang Yang, Ke Yang, Hong-Liang Cui, Weiling Fu, *Biomedical Optics Express* **8**(10), 4427 (2017).
- [10] F. Yan, L. Li, R. X. Wang, *Journal of Lightwave Technology* **37**(4), 1103 (2019).
- [11] Shih-Ting Huang, Shen-Fu Hsu, Kai-Yuan Tang, Ta-Jen Yen, Da-Jeng Yao, *Micromachines* **11**(1), 74 (2020).
- [12] Yogesh Kumar Srivastava, Apoorva Chaturvedi, Manukumara Manjappa, Abhishek Kumar, Govind Dayal, Christian Kloc, Ranjan Singh, *Advanced Optical Materials* **4**(3), 457 (2016).
- [13] X. Hu, G. Q. Xu, L. Wen, *Laser & Photonics Reviews* **10**(6), 962 (2016).
- [14] Z. X. Geng, X. Zhang, Z. Y. Fan, *Scientific Reports* **7**(1), 16378 (2017).
- [15] Y. J. Zhang, S. F. Wang, G. C. Zhong, *Chinese Journal of Lasers* **46**(6), 0614038 (2019).
- [16] L. Liang, L. Wen, C. P. Jiang, *Infrared and Laser Engineering* **48**(2), 0203001 (2019).
- [17] L. Q. Cong, S. Y. Tan, R. Yahiaoui, *Applied Physics Letters* **106**(3), 031107 (2015).
- [18] Aronika Jindal, Shruti Sobti, Mukesh Kumar, Siddharth Sharma, Manoj Kumar Pal, *IEEE Sensors Journal* **10**, 3705 (2016).
- [19] N. Ayyanar, G. Thavasi Raja, Mohit Sharma, D. Sriram Kumar, *IEEE Sensors Journal* **17**, 7093 (2018).
- [20] X. Wang, J. L. Wang, *Acta Optica Sinica* **40**(19), 1904001 (2020).
- [21] Feng Lan, Feng Luo, Pinaki Mazumder, Ziqiang Yang, Lin Meng, Zhengqiang Bao, Jun Zhou, Yaxin Zhang, Shixiong Liang, Zongjun Shi, Abdur Rauf Khan, Ziqi Zhang, Luyang Wang, Jing Yin, Hongxin Zeng, *Biomedical Optics Express* **10**(8), 3789 (2019).
- [22] Rui Zhang, Qingming Chen, Kai Liu, Zefeng Chen, Kaidi Li, Xuming Zhang, Jianbin Xu, *IEEE Transactions on Terahertz Science and Technology* **2**, 209 (2019).
- [23] Yang Jiping, Wang Minchang, De Hu, Kang Ying, *Journal of Optics* **23**(41), 2328001-1 (2021).

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