研究论文

光学学报

基于双开口环结构的太赫兹超材料生物传感器

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摘要 为了拓展超材料在太赫兹波段的生物传感应用，设计了一种双开口环结构的太赫兹超材料生物传感器，通过两个等效电容电感（LC）谐振实现了高折射率灵敏度传感。首先，使用有限积分技术（FIT）数值计算了该传感器的太赫兹光谱，并对其进行了结构尺寸优化。然后，在传感器表面放置了一层折射率可变的分析物，通过对不同透射光谱的计算分析，验证了该传感器具备 161.06 GHz/RIU（RIU 为折射率单位）的折射率灵敏度和 1.98 的品质因素（FOM）值。最后，采用传统光刻技术和剥离工艺在石英衬底上制作铜金属结构，制备了该传感器，利用其对牛血清白蛋白（BSA）溶液进行了实际测试，实验得到传感灵敏度为 59.02 GHz/(ng·mm^{-2})和检测下限为 0.004 mg/mL。

关键词 传感器；生物传感器；太赫兹超材料；双开口环结构

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1 引　　言

由于太赫兹波具有可实现大分子指纹识别[1-2]、低光子能量和高穿透性等特性，故已成为研究化学和生物分子的一种十分有应用前景的技术[3-4]。传统的生物检测方法（聚合酶链反应[2,5]、荧光显微镜[6-7]和流式细胞术[8-9]等）具有需要标记、过程长、成本高、程序复杂和灵敏度有限等特点。随着太赫兹时域光谱和便携式太赫兹光谱工具的发展，太赫兹传感技术在高灵敏度和现场检测/识别微量生物分子、促进蛋白质合成和细胞分裂等领域中的应用越来越广泛[10-11]。然而，生物分子/细胞与太赫兹波长（30 μm～3 mm）之间的尺寸不匹配会导致散射截面小和吸收弱，故需要利用亚波长尺度的增强太赫兹谐振来实现强光捕获。由于超材料可以通过人为设计来实现电磁波的调控，故可以起到增强太赫兹波检测的效果[12-14]。

本文设计了一种双开口环结构太赫兹超材料生物传感器，通过两个电容电感（LC）谐振[15-16]在 0.776 THz 处产生一个透射谷。通过软件数值仿真和计算证明该传感器具备 161.06 GHz/RIU（RIU 为折射率单位）的折射率灵敏度和 1.98 的品质因素（FOM）值，并加工制作了该生物传感器来进行牛血清白蛋白（BSA）质量浓度检测实验。实验得到了 59.02 GHz/(ng·mm^{-2})的 BSA 检测灵敏度，且检测下限为 0.004 mg/mL。

2 设计与仿真

2.1 结构设计

所设计的双开口环结构太赫兹超材料生物传感器如图 1(a)所示。该结构单元包含一组双金属开口环，两个金属开口环开口方向相同，且关于 y 轴对称。金属材料为铜，每个金属开口环都制作在大石英衬底（折射率为 $n=1.95$）上[17-18]。图 1(a)右下角的插图显示了单元结构图，每个金属开口环的外长 l 和线宽 w 分别为 42 μm 和 8 μm，开口长度 g 和开口环间距 s 分别为 10 μm 和 19 μm。金属的厚度为 0.2 μm，周期尺寸 P_x 和 P_y 为 140 μm 和 140 μm。

2.2 仿真结果与分析

使用电磁仿真软件 CST 对所设计模型进行仿真计算[19]。首先，对设计的双开口环结构太赫兹超材料生物传感器进行透射光谱的仿真，仿真的波段在 0.5～0.9 THz。图 1(b)所示为从接收端处得到的透射光谱。可以发现：仿真得到的透射谱强烈依赖于入射电磁波的频率；在 0.776 THz 处可以观察到一个明显的透射谷，且表现出左右对称的线形。为了更深入地了解这个频率处的谐振原理，仿真研究了超材料传感器在这个频率处的电场和表面电流。如图 2 所示，当谐振频率为 0.776 THz 时，在两个金属开口环上都会形成一个逆时针方向旋转的表面电流，并且会导致电荷聚集在金属开口环两端，此时金属开口环的金属结构就等效于电感 L，而金属开口环的开口就等效于电容
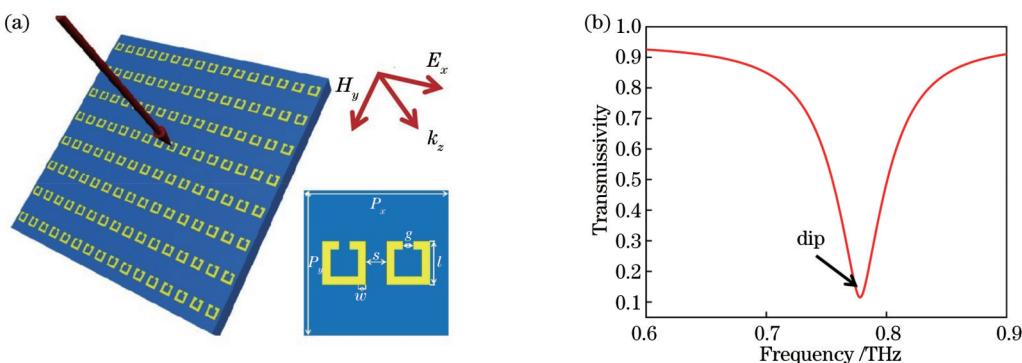
图 1 双开口环结构太赫兹超材料生物传感器的结构示意图和太赫兹透射光谱。(a)结构示意图;(b)太赫兹透射光谱

Fig. 1 Structural diagram and terahertz transmission spectrum of terahertz metamaterial biosensor with double split-ring structure. (a) Structural diagram; (b) terahertz transmission spectrum

C,两者形成 LC 振荡电路。具体 LC 谐振电路模型如图 2(c)所示。由于这是两个轴对称的金属开口环,故这两个金属开口环可以等效于相同的 LC 谐振电路,

振荡频率为 $f = \left(2\pi\sqrt{LC}\right)^{-1}$。因此,可以通过改变 L 和 C 来改变生物传感器的谐振频率。
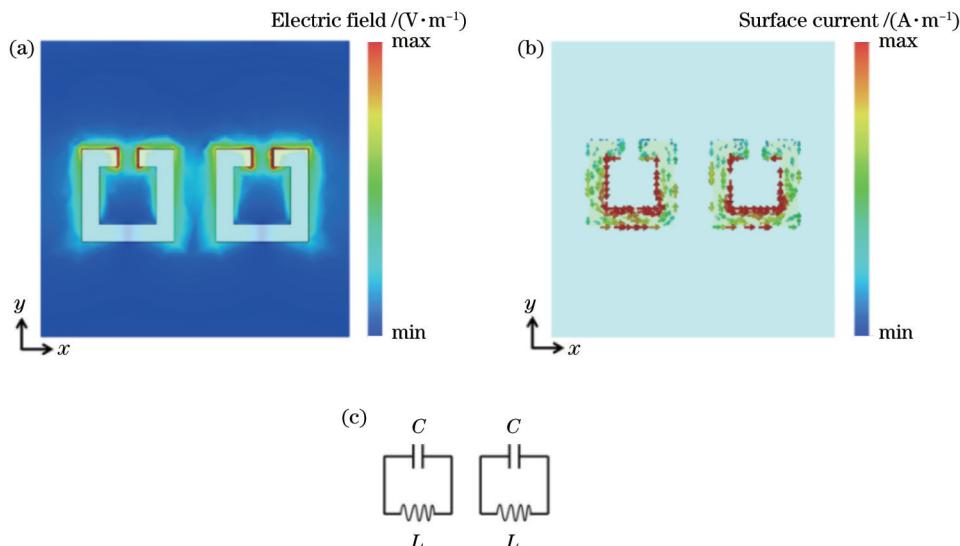
图 2 双开口环结构太赫兹超材料生物传感器在 0.776 THz 处的电场图、表面电流图和 LC 谐振模型图。(a)电场图;(b)表面电流图;(c)LC 谐振模型图

Fig. 2 Electric field diagram, surface current diagram and LC resonance model diagram of terahertz metamaterial biosensor with double split-ring structure at 0.776 THz. (a) Electric field diagram; (b) surface current diagram; (c) LC resonance model diagram

进一步研究了超材料单元结构周期尺寸的变化对透射谷谐振频率的影响,结果如图 3 所示。可以发现:当 P_x 增加时,谐振谷发生蓝移;当 P_y 增加时,谐振谷也表现出蓝移。由此可得,超材料是一种亚波长周期结构材料,谐振频率与超材料单元结构的周期尺寸密切相关。然而,由于该生物传感器的谐振谷源于两个相同的 LC 谐振,故周期尺寸发生变化时对 LC 谐振的影响很小,这会导致周期尺寸发生变化时,谐振谷频率的变化很小。

超材料生物传感器的谐振频率和 LC 谐振密切相关,可以通过改变开口环的结构参数来改变谐振频率。因此,对超材料金属单元结构尺寸的变化与透射谷谐振频率之间的关系进行了研究,结果如图 4 所示。可

以发现:当 g 增加时,谐振谷发生蓝移;当 s 增加时,谐振谷表现出蓝移;当 w 增加时,谐振谷也出现蓝移;只有当 l 增加时,谐振谷才发生红移。从各个结构尺寸变化对应的透射光谱可以看出,所设计的双开口环结构太赫兹生物传感器的谐振频率对 g、l 和 w 三个结构尺寸的变化更为敏感,对结构尺寸 s 的变化并不敏感。这可以理解为两个 LC 谐振之间距离的变化对 LC 谐振影响很小,只有电容和电感本身的尺寸变化才会对 LC 谐振的谐振频率产生较大影响。

研究入射角和偏振角变化对超材料透射光谱的影响也很重要。在 CST 仿真模型中设置电磁波垂直入射,偏振模式为横磁(TM),然后改变入射角和偏振角。这些角度变化的定义如图 5(a)所示。入射角变
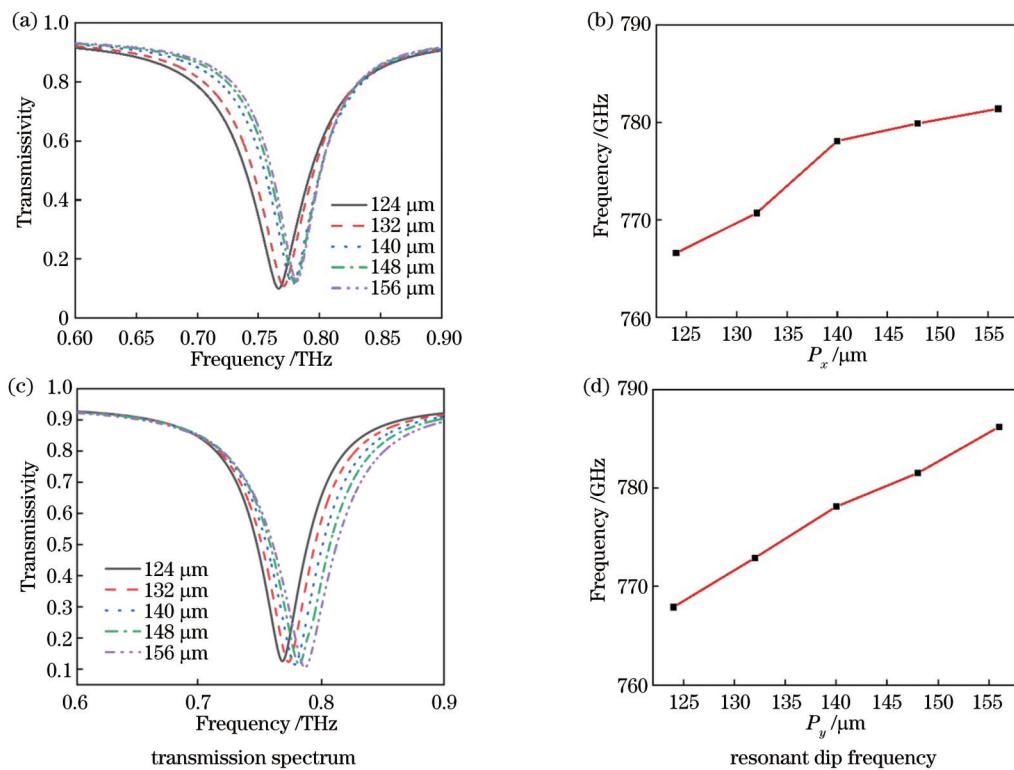
图 3　单元结构周期尺寸变化对生物传感器透射谱与谐振谷频率的影响。(a)(b)P_x;(c)(d)P_y

Fig. 3　Influence of periodic size variation of cell structure on transmission spectrum and resonant dip frequency of biosensor. (a)(b) P_x; (c)(d) P_y

化是指 xz 平面上的 θ_i 变化,偏振角变化是指 xy 平面上的 θ_p 变化。如图 5(b)、(c)所示:当入射角和偏振角在 0°~30°之间变化时,谐振频率和透射率几乎没有变化;当入射角和偏振角大于 30°时,谐振频率和透射率发生了较为明显的改变。可以看出,所设计的超材料传感器的谐振频率和透过率在 0°~30°保持了良好的稳定性,在该范围内展示出了良好的角度不敏感性,这种一定范围内的不敏感特性有利于生物传感器的实际应用。

为探索所设计的双开口环结构太赫兹超材料生物传感器的传感性能,一层 20 μm 厚的薄层分析物被添加到该太赫兹超材料生物传感器的表面上,如图 6(a)所示。如图 6(b)所示,通过线性改变表面分析物的折射率,模拟得到了该超材料生物传感器在不同分析物折射率下的透射光谱。从仿真结果可以看到,随着折射率的增加,谐振谷发生了红移,谐振频率开始减小。然后,收集每个分析物折射率对应的谐振峰频率。通过线性拟合,最终得到了图 6(c)中的拟合结果,表明该双开口环结构太赫兹超材料生物传感器具备 161.06 GHz/RIU 的折射率灵敏度,并且 FOM 的计算值为 1.98,其中 R^2 是拟合度。

不同介电常数的衬底材料对生物传感器的折射率灵敏度影响也很大。仿真了衬底为硅(介电常数为 11.9)[19]情况下双开口环结构太赫兹超材料生物传感器的折射率灵敏度。在 CST 电磁仿真软件模型中,衬底被换成介电常数更大的硅材料,仿真了在不同分析物折射率下的透射光谱,结果如图 7(a)所示。当分析物折射率为 1.0 时,谐振频率偏移到了 0.472 THz 处。然后,分析拟合分析物不同折射率与对应谐振频率的关系,如图 7(b)所示,计算得到的折射率灵敏度为 37.8 GHz/RIU,计算得到的 FOM 值为 0.687。相比于石英衬底,换成介电常数更大的硅衬底后双开口环结构太赫兹超材料生物传感器的折射率灵敏度和 FOM 值都发生了明显下降。因此,最终选择石英作为衬底材料来进行下一步的实验制作与测试。

继续探究了开口环对超材料生物传感器折射率灵敏度的影响,经过仿真和计算得到了单开口环生物传感器的折射率灵敏度。图 8(a)为不同折射率分析物对单开口环生物传感器透射光谱的影响。可以看出,与双开口环相比,单开口环并没有使谐振频率产生较大的偏移。然而,从图 8(b)所示的折射率灵敏度拟合曲线中可以看出,单环超材料的灵敏度为 148 GHz/RIU,低于双环超材料的 161.06 GHz/RIU。因此,最终采用双开口环超材料。

3　传感器的制备及实验

该生物传感器可以通过传统的光刻技术加剥离工艺制作。首先,在 2 mm 厚的石英衬底上旋涂一层 AZ5214 光刻胶,转速为 2000 r/min。然后,在 110 ℃的热板上烘烤 90 s,在稍微冷却后,就可以进行曝光和显
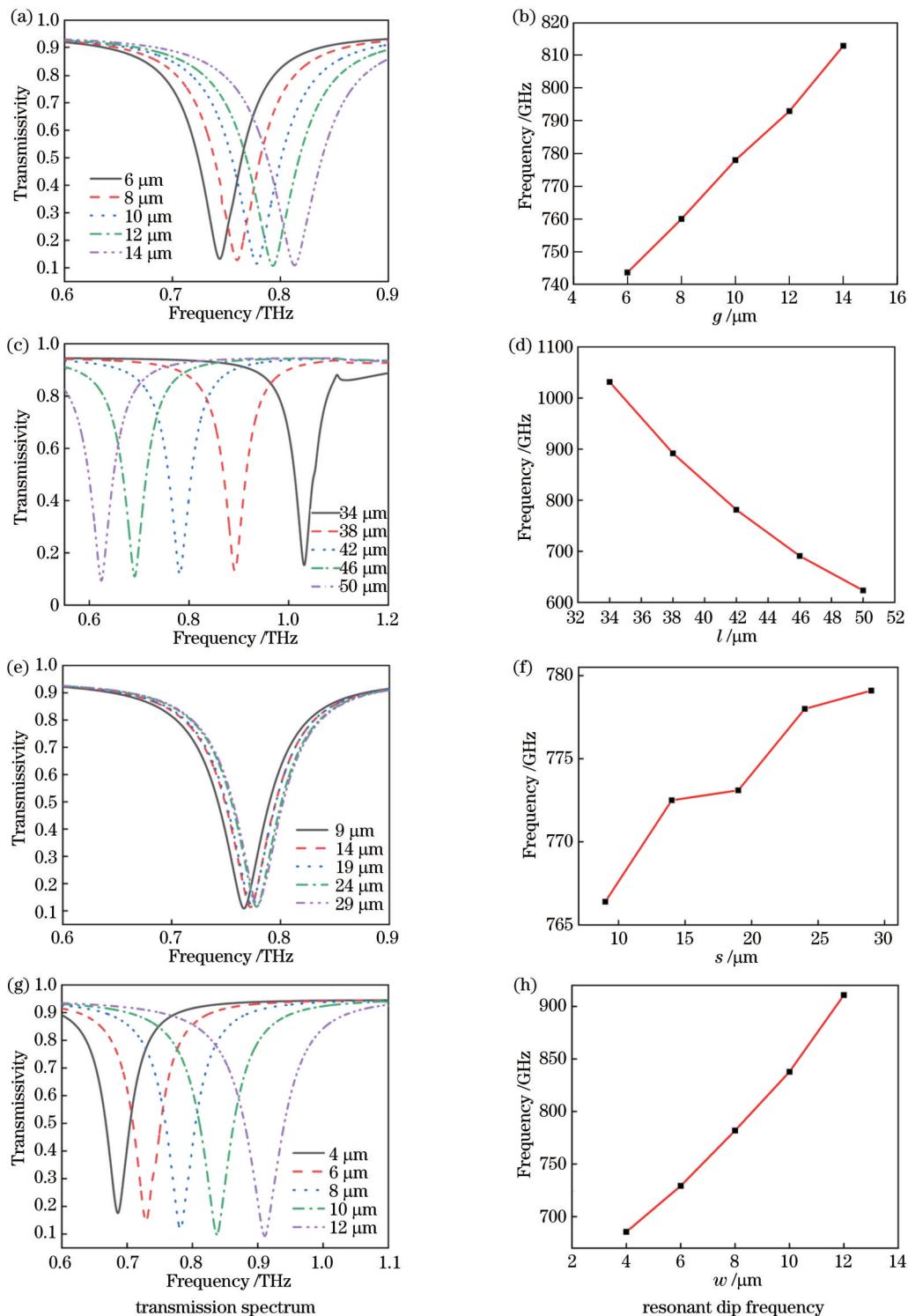
图 4 开口环的结构参数变化对生物传感器透射谱与谐振谷频率的影响。(a)(b) g；(c)(d) l；(e)(f) s；(g)(h) w

Fig. 4 Influence of structural parameters of split-ring on transmission spectrum and resonant dip frequency of biosensor. (a)(b) g; (c)(d) l; (e)(f) s; (g)(h) w

影，显影液是质量浓度为 0.01 g/mL 的氢氧化钠溶液。将片子在溶液中浸泡 20 s 后，清洗干净就可以进行镀膜，在片子上表面镀上一层金属铜。接着，进行剥离，用丙酮作为剥离液，配合超声波震荡仪进行剥离。最后，可得到双开口环结构太赫兹超材料生物传感器。完成的双开口环结构太赫兹超材料生物传感器的显微

镜图像如图 9 所示，其金属结构区域尺寸为 12 mm×12 mm。

在生物检测实验中所用的 BSA 购买自 Sigma-Aldrich 公司。将无水磷酸氢二钠（Na_2HPO_4）和无水磷酸二氢钠（NaH_2PO_4）混合来配置磷酸盐缓冲液（PBS），PBS 是生物化学研究中广泛使用的一种缓冲
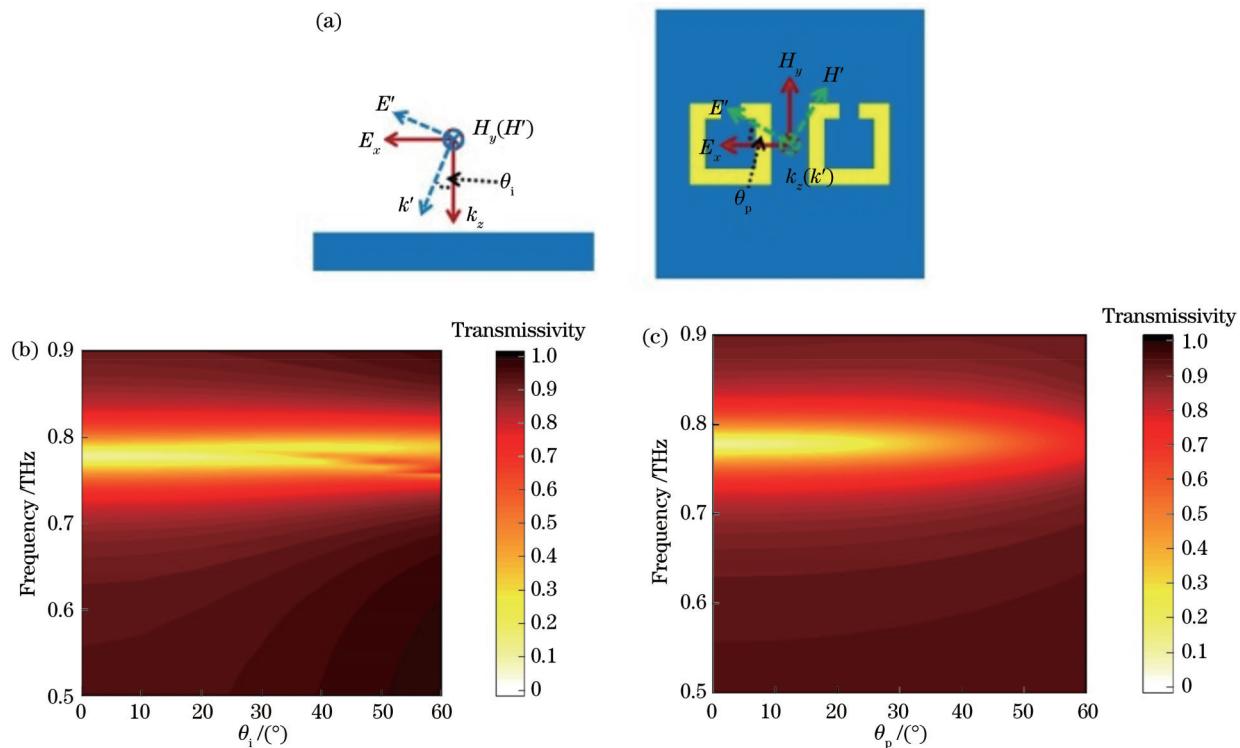
图 5 入射角 θ_i 和偏振角 θ_p 对透射光谱的影响。(a) CST 仿真时的角度方向定义；(b)入射角变化对谐振频率和透射率的影响；(c)偏振角变化对谐振频率和透射率的影响

Fig. 5 Influence of incident angle θ_i and polarization angle θ_p on transmission spectrum. (a) Angle direction definition during CST simulation; (b) influence of incident angle variation on resonance frequency and transmissivity; (c) influence of polarization angle variation on resonance frequency and transmissivity
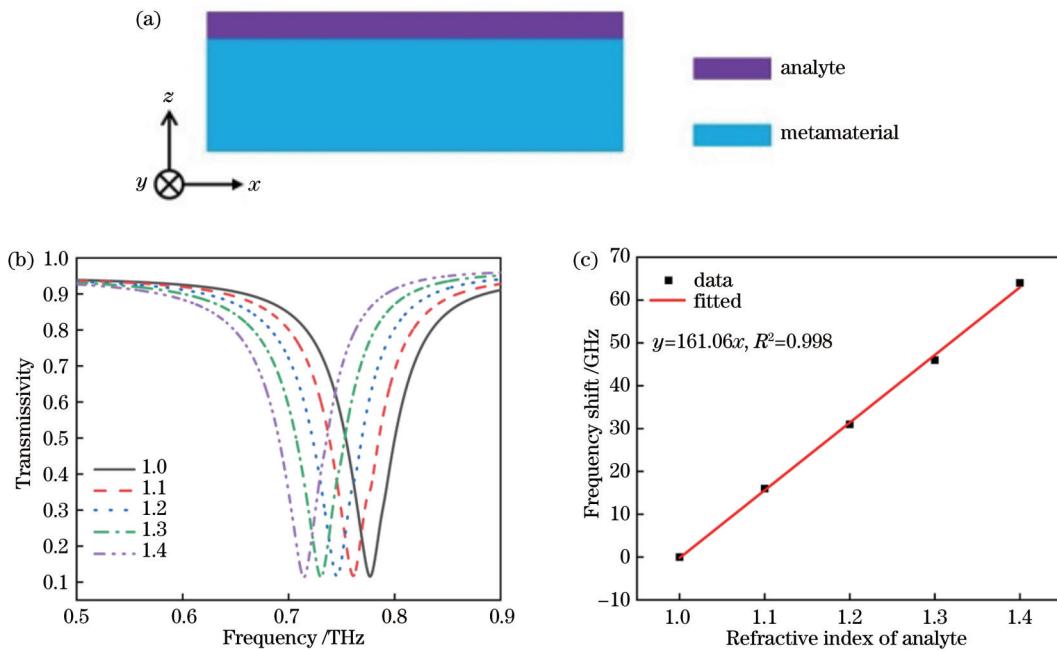
图 6 分析物折射率变化对生物传感器谐振频率的影响。(a)生物传感器结构示意图；(b)随折射率变化的透射光谱；(c)折射率灵敏度拟合曲线

Fig. 6 Influence of refractive index variation of analyte on resonance frequency of biosensor. (a) Structural diagram of biosensor; (b) transmission spectrum varying with refractive index; (c) fitting curve of refractive index sensitivity

液，能够保持溶质中生物分子的活性，所配置的各个质量浓度的待测 BSA 溶液的溶剂均为 PBS 缓冲液。不

同生物分子对缓冲液的 pH 值要求不同，可以通过调节无水磷酸氢二钠溶液和无水磷酸二氢钠溶液的配比
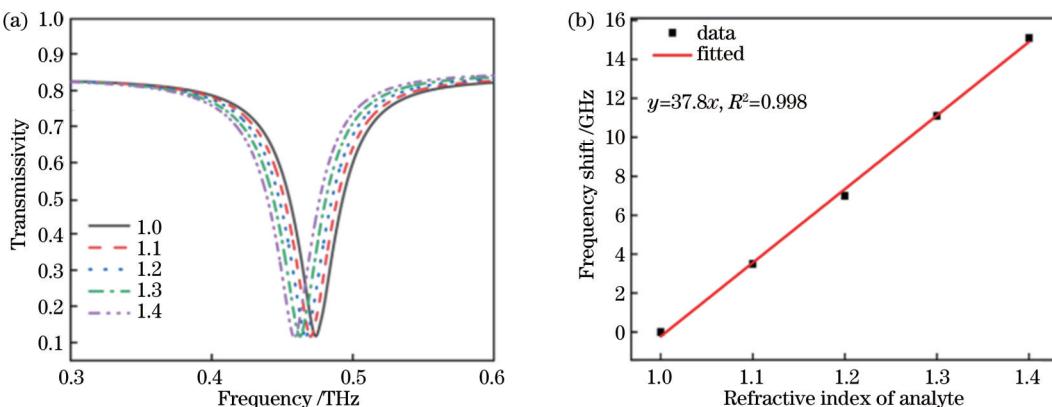
图 7 衬底为硅时分析物折射率变化对生物传感器谐振频率的影响。(a)随折射率变化的透射光谱;(b)折射率灵敏度拟合曲线

Fig. 7 Influence of refractive index variation of analyte on resonance frequency of biosensor with substrate of silicon. (a) Transmission spectrum varying with refractive index; (b) fitting curve of refractive index sensitivity
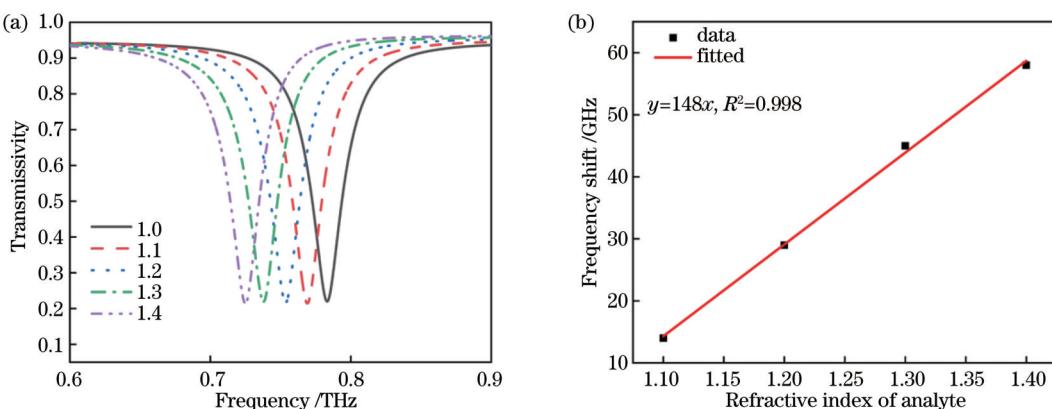

图 8 单开口环时分析物折射率变化对生物传感器谐振频率的影响。(a)随折射率变化的透射光谱;(b)折射率灵敏度拟合曲线

Fig. 8 Influence of refractive index variation of analyte on resonance frequency of biosensor with single split-ring structure. (a) Transmission spectrum varying with refractive index; (b) fitting curve of refractive index sensitivity
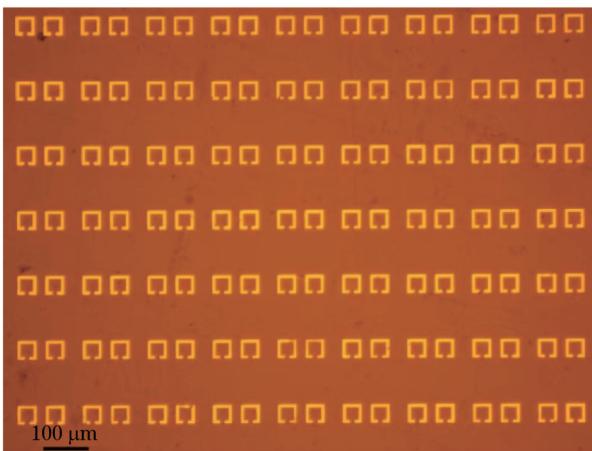
图 9 双开口环结构太赫兹超材料生物传感器显微镜图

Fig. 9 Micrograph of terahertz metamaterial biosensor with double split-ring structure

来配置不同 pH 值的缓冲液,以适应不同生物分子的需求,具体比例如表 1 所示。BSA 溶液一般需要 pH 值在 7.4 左右,故最终选定配置了 pH 为 7.4 的 PBS 作为溶剂来配制不同质量浓度的 BSA 溶液。

最终配制的 BSA 溶液的质量浓度分别为 0.1、0.5、4.0 mg/mL。在所有溶液的配制过程中,均使用高精密度电子天平来保证配置的精度,并且不同质量浓度的 BSA 溶液采用梯度配制法。通过液相沉积法将分析物添加到生物传感器表面上。每次使用移液枪将 150 μL 的 BSA 溶液转移到生物传感器表面,并在 40 ℃的加热台上干燥生物传感器。当生物传感器在 40 ℃温度下进行加热时,蛋白质膜形成更快且更均匀。当 BSA 溶液滴加在生物传感器表面时,受到水表面张力的影响,溶液停留在该生物传感器的表面上,加热和干燥后会形成一层 BSA 薄膜。每次在滴加下一个质量浓度的 BSA 溶液之前,生物传感器都会被放在去离子水中并使用超声波振动器来清洗,以确保前一过程中的蛋白质膜被清除,从而保证该生物传感器的表面清洁而不影响下一个质量浓度 BSA 溶液的测量。

使用连续波太赫兹光谱系统(Toptica Photonics AG,TeraScan 1550)进行所有光谱测量。该系统由双激光控制(DLC)智能电子设备、2 个分布式反馈

pH	Volume of Na_2HPO_4 with mass concentration of 0.2 mol·L^{-1} /mL	Volume of NaH_2PO_4 with mass concentration of 0.2 mol·L^{-1} /mL
6.5	31.5	68.5
6.6	37.5	62.5
6.7	43.5	56.5
6.8	49.0	51.0
6.9	55.0	45.0
7.0	61.0	39.0
7.1	67.0	33.0
7.2	72.0	28.0
7.3	77.0	23.0
7.4	81.0	19.0
7.5	84.0	16.0
7.6	87.0	13.0
7.7	89.5	10.5
7.8	91.5	8.5
7.9	93.0	7.0
8.0	94.7	5.3

（DFB）激光器、2 个光纤耦合 InGaAs 光混合器和 4 个 90°离轴抛物面镜组成，如图 10 所示。利用 90°离轴抛物面镜准直太赫兹波并聚焦在样品上。该仪器通过两个分布式反馈激光器在光混合器中混频来产生一个频率在两束激光器差频处的光拍，混频后的激光被分成两束，一束作为发射太赫兹波，一束送入接收器中作为探测光。本仪器所用的两个激光器的波长可以通过 DLC 智能器件进行温度调节，由于温度可以实现微小的变化，故差频最小可以以兆赫兹精度进行调节[20]。在 50～1220 GHz 之间以 743 MHz 的步长进行扫描，并在快速扫描模式下以 10 ms 积分时间进行操作，以减少扫描时间，从而获得所有的传输光谱。
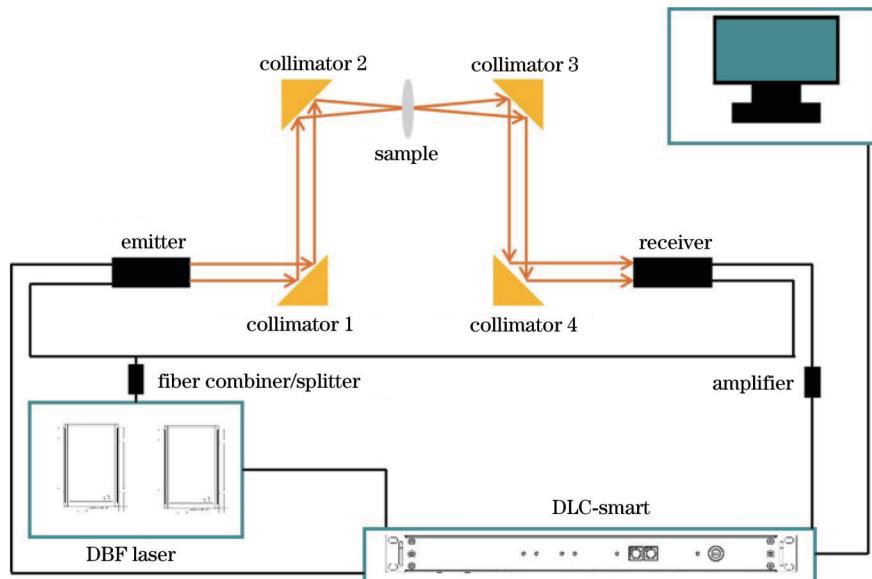

图 10 连续波太赫兹光谱系统示意图
Fig. 10 Schematic diagram of continuous wave terahertz spectrum system

双开口环结构太赫兹超材料生物传感器的蛋白质检测实验在 4 种质量浓度的 BSA 溶液中进行。在整个实验过程中，按从低到高的顺序添加每组 BSA 溶液。所有测量过程重复 3 次，最终的测量结果如图 11 (a)所示。随着 BSA 溶液质量浓度的增加，谐振谷发生红移，谐振频率随之减小，这一趋势与软件数值计算结果一致。谐振谷强度的变化是由 BSA 蛋白吸收了太赫兹波造成的。从测试结果可以看到，谐振谷的频

移与 BSA 溶液质量浓度之间的关系不是线性的,这在生物学实验中很常见[21-22]。通常 Hill 模型[23]被用来拟合谐振频率变化和 BSA 溶液质量浓度的关系曲线,故

其可以用来表征所设计的超材料生物传感器与生物分子之间的结合能力。因此,使用 Hill 模型来拟合实验数据,如图 11(b)所示。
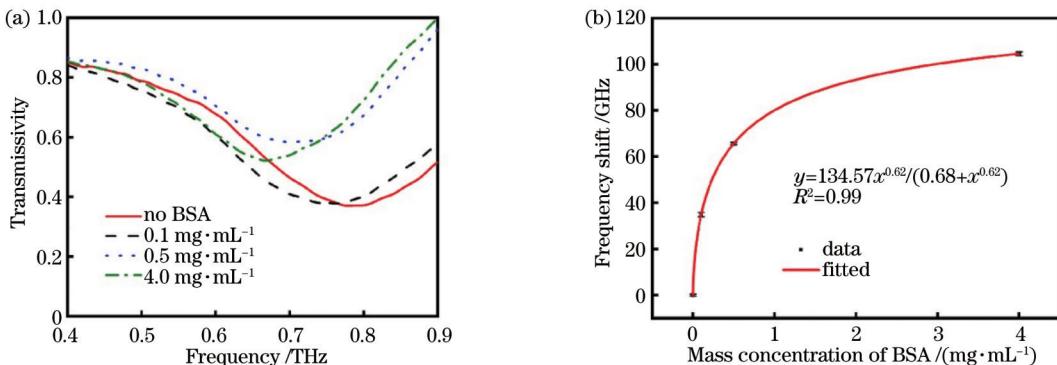
图 11 不同 BSA 溶液下生物传感器的透射光谱和 Hill 拟合结果。(a)透射光谱;(b)Hill 拟合曲线

Fig. 11 Transmission spectra and Hill fitting results of biosensor under different BSA solutions. (a) Transmission spectrum; (b) Hill fitting curve

Hill 方程为

$$\Delta f = \Delta f_{\max} \cdot \frac{C_{\mathrm{BSA}}^n}{K_{\mathrm{D}} + C_{\mathrm{BSA}}^n}, \quad (1)$$

式中:最大峰值频移 $\Delta f_{\max}$ 是饱和值;C_{BSA} 是 BSA 溶液的质量浓度;n 是希尔系数;K_{D} 是离解常数。

由图 11(b)所示的拟合曲线可知,希尔系数 n 为 0.62,解离常数 K_{D} 为 0.68 mg/mL。此外,$\Delta f_{\max}$ 约为 134.57 GHz,这代表饱和质量浓度下的最大峰值频移。谐振谷频率与 BSA 溶液质量浓度的希尔拟合结果证实了实验的可靠性和准确性。

然后,可以进一步计算传感器的生物传感灵敏度,生物传感器的灵敏度 S[24]的计算公式为

$$S = \frac{\Delta f_{\max}}{\delta_{\max}}, \quad (2)$$

式中:$\Delta f_{\max} = 134.57$ GHz;$\delta_{\max}$ 为 BSA 的表面密度。$\delta_{\max}$[24]的计算公式为

$$\delta_{\max} = \frac{M_{\mathrm{BSA}}}{N_{\mathrm{A}} \times P_{\mathrm{BSA}}^2}, \quad (3)$$

式中:$M_{\mathrm{BSA}} = 66430$ g/mol 是 BSA 的相对分子质量[25];$N_{\mathrm{A}} = 6.02 \times 10^{23}$ mol^{-1} 是阿伏伽德罗常数;$P_{\mathrm{BSA}} = 6.96$ nm 是一个 BSA 分子的平均长度[26]。计算可得 $\delta_{\max}$ 为 2.28 ng/mm^2,最终可计算得出生物传感器的 BSA 检测灵敏度为 59.02 GHz/(ng·mm^{-2})。
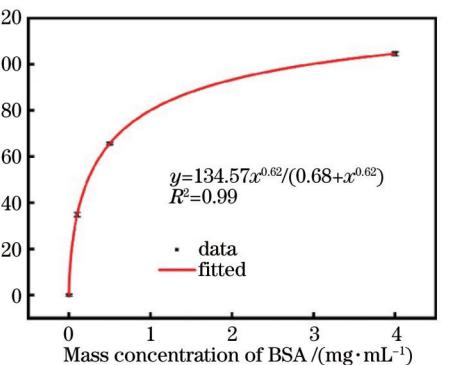
使用 Hill 模型获得的 K_{D} 表明,离解常数与 BSA 密切相关,BSA 的检测限(LOD)$C_{\lim}$[27]的计算公式为

$$C_{\lim} = K_{\mathrm{D}} \times \frac{S_{\mathrm{f}}}{\Delta f_{\max} - S_{\mathrm{f}}}, \quad (4)$$

式中:S_{f} 为光谱分辨率,其值为 743 MHz。式(4)表明,较小的离解常数会导致较低的检测限。因此,计算得出 $C_{\lim}$ 为 0.004 mg/mL。

图 12 为不同 BSA 溶液下生物传感器透射谷幅值随 BSA 质量浓度变化的曲线图。可以看出,随着 BSA

质量浓度的增大,透射谷的幅值呈现出先增大后减小的变化趋势,规律性较弱,故采用检测透射频率的变化对分析物质量浓度进行检测。
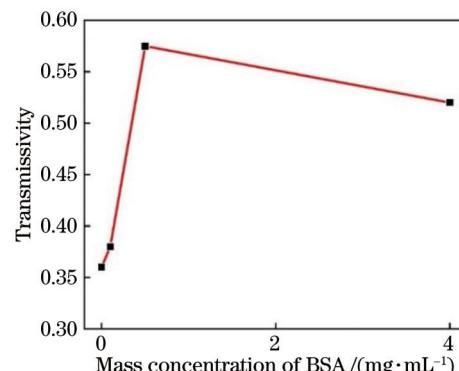
图 12 不同质量浓度 BSA 溶液下生物传感器的透射率变化图

Fig. 12 Transmissivity variation diagram of biosensor under BSA with different mass concentrations

4 结 论

设计了一种双开口环结构太赫兹超材料生物传感器,其由石英衬底和表面铜金属周期单元结构组成。太赫兹波垂直入射在生物传感器表面时会激发出两个对称的 LC 谐振,在接收端的透射光谱中表现为一个频率在 0.766 THz 处的透射谷。通过理论仿真可得到该生物传感器的折射率灵敏度为 161.06 GHz/RIU,且 FOM 值为 1.98。然后,对设计的生物传感器进行了实验制作,并对其进行了 BSA 质量浓度检测实验,最终得到了 59.02 GHz/(ng·mm^{-2})的 BSA 检测灵敏度,且最低检测下限为 0.004 mg/mL。理论仿真和生物实验的结果都证明,该生物传感器具有良好的传感性能。该生物传感器结构简单小巧且性能稳定,可用于痕量生物分子的快速检测和相关应用领域中。

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Terahertz Metamaterial Biosensor Based on Double Split-Ring Structure

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Abstract

Objective　Terahertz wave has become a promising technology for studying chemical and biological molecules due to its macromolecular fingerprint recognition, low photon energy, and high penetration characteristics. With the development of terahertz time-domain spectroscopy and portable terahertz spectroscopy tools, terahertz sensing technology is increasingly widely used in the fields of high sensitivity and on-site detection/recognition of trace biological molecules, promotion of protein synthesis, and cell division. However, there are problems such as low scattering cross-section and weak absorption due to the size mismatch between biomolecules/cells and terahertz wavelengths (30 μm−3 mm). Therefore, it is necessary to use enhanced terahertz resonance with subwavelengths to achieve strong light capture. Besides, metamaterials can be artificially designed to control electromagnetic waves, which can enhance the detection ability of terahertz waves.

Methods　From previous studies, it has been found that under the illumination of the incident light, the metamaterial with a metal split-ring structure will generate a very local and binding electric field at the split position so that it can greatly enhance the absorption cross-section of the biochemical detection sample located on the surface of the split-ring structure and realize the sensing detection of trace biochemical samples. Based on the analysis of metamaterials with a split-ring structure, a quartz substrate terahertz metamaterial biosensor with a double split-ring structure is designed in this paper. Through the frequency change of two equivalent capacitance inductor (LC) resonances in different refractive index environments, high refractive index sensitivity sensing is realized, and the detection of some biological molecules with different concentrations is achieved.

Results and Discussions　Firstly, the terahertz transmission spectrum of the sensor is numerically calculated using the finite integration technique (FIT), and there is an obvious resonance transmission dip at 0.776 THz (Fig. 1). Then, the influence of each structural parameter on the resonant frequency is analyzed, and the variation law of the resonant dip frequency with the structural parameters is obtained. At the same time, in order to investigate the applicability of the sensor, the influence of different incident angles and polarization angles on the sensor is further studied. It is found that the position of the resonant frequency and the transmittance is almost unchanged in the range of 0°−30°, which indicates that the sensor is very appropriate for the practical application of biological sensing. In order to further analyze the sensing performance of the sensor, this paper places a layer of the analyte with a variable refractive index on the surface of the sensor. Through the calculation and analysis of its different transmission spectra, it is found that with the increase in the refractive index, the resonance dip has a red shift, and the resonant frequency gradually decreases. After collecting the resonance peak frequency corresponding to the refractive index of each analyte, it is verified that the sensor has a refractive index sensitivity of 161.06 GHz/RIU (refractive index unit) and a figure of merit (FOM) value of 1.98 (Fig. 6) calculated by linear fitting. In order to investigate the influence of different cell numbers and substrate materials on the sensor's characteristics, the performance of the single split-ring sensor with the same structural parameters and the double split-ring sensor with silicon material as the substrate is compared. It is found that the refractive index sensitivity of the two sensors is lower than that of the double split-ring sensor designed in this paper. Finally, in order to verify the actual performance of the terahertz biosensor, the designed copper metal structure is fabricated on the quartz substrate by using the traditional photolithography technology and stripping process, and the sensor is successfully fabricated (Fig. 9). By using the continuous wave terahertz spectrum detection system (Topica Photonics AG, TeraScan 1550), the sensor is tested on different mass concentrations of bovine serum albumin (BSA) solution (Table 1), and the experimental results are shown in Fig. 11. The experimental results show that with the increase in mass concentration of BSA solution, the resonance dip has a red shift, and the resonant frequency decreases, which is consistent with the numerical results. However, the relationship between the frequency shift of the resonance dip and the mass concentration of the BSA solution is not linear, which is common in biological experiments. The Hill model is usually used to fit the relationship curve between the change of resonant frequency and the mass concentration of BSA solution. By using this model to fit the experimental results, the sensing sensitivity of 59.02 GHz/(ng·mm^{-2}) and the detection limit of 0.004 mg/mL are obtained.

Conclusions　In this paper, a quartz substrate terahertz metamaterial biosensor with a double split-ring structure is designed and fabricated. It is found that there is an obvious resonance transmission dip at 0.776 THz (Fig. 1). The influence of different incident angles and polarization angles on the sensor is further studied. It is found that the position of

the resonant frequency and the transmittance is almost unchanged in the range of 0°–30°. This paper also places a layer of the analyte with a variable refractive index on the surface of the sensor, and it is found that the sensor has a refractive index sensitivity of 161.06 GHz/RIU and a FOM value of 1.98 (Fig. 6). At last, the sensor is tested in different mass concentrations of BSA solution (Table 1), and the experimental results are shown in Fig. 11. By using Hill model to fit the experimental results, the sensing sensitivity of 59.02 GHz/(ng·mm^{-2}) and the detection limit of 0.004 mg/mL are obtained. The results of theoretical simulation and biological experiments show that the biosensor has good sensing performance, simple structure, small size, and stable performance. It can be used for the rapid detection of trace biomolecules and related application fields.

Key words sensors; biosensors; terahertz metamaterials; double split-ring structure