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· 综述 ·

太赫兹光谱技术在口腔微生物检测中的研究进展

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【摘要】 微生物与人类健康关系密切,其致病性是多种感染性疾病的重要病因,尤其在口腔医学中表现为龋病、牙周病及口腔黏膜病等常见疾病。精准、快速的微生物检测是疾病早期诊断、靶向治疗及疾病预防的关键。传统方法如细菌培养、分子生物学检测等虽具特异性,但受检测周期长、操作流程复杂及实验条件依赖性强等限制。太赫兹(terahertz, THz)光谱技术因其非电离性、高灵敏度以及对水分子和生物大分子的特异性响应,在微生物检测领域展现出重要的应用潜力。结合THz时域光谱、近场成像及超材料增强技术,研究表明该方法能够有效区分细菌、真菌和酵母菌等不同微生物类型,甚至可鉴别革兰氏阳性与阴性细菌,以及判断细菌的存活状态。并通过机器学习提升了该方法信号特征提取与分类的准确性,在多类别微生物识别、耐药菌株判别及微生物浓度定量等方面表现出显著优势。然而,目前THz技术仍受水分强吸收、穿透深度有限以及缺乏标准化光谱数据库等问题制约,未来亟须在降低水分干扰、提升复杂样本检测能力及建立统一的微生物光谱标准方面持续突破。本文系统综述了THz技术在微生物检测中的最新进展,分析了技术机理、优势及临床转化挑战,并提出未来研究方向。

【关键词】 太赫兹光谱; 微生物; 太赫兹时域光谱; 太赫兹近场成像; 热曲线; 超材料; 成像; 机器学习; 微生物检测

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【Abstract】 Microorganisms are closely associated with human health, and their pathogenicity is a key factor in various infectious diseases, particularly in dentistry, where they contribute to common conditions such as dental caries, periodontitis, and oral mucosal diseases. Accurate and rapid microbial detection is crucial for early diagnosis, targeted therapy, and disease prevention. Conventional methods, including bacterial culture and molecular biological assays, offer specificity but are limited by long detection cycles, complex procedures, and dependence on laboratory conditions. Terahertz (THz) spectroscopy has emerged as a promising tool in microbial detection due to its non-ionizing nature, high sensitivity, and specific responses to water molecules and biomacromolecules. Integrating THz time-domain spectroscopy, near-field imaging, and metamaterial-enhanced techniques, studies have demonstrated the ability of this approach to effectively distinguish bacteria, fungi, and yeast, differentiate gram-positive and gram-negative bacteria, and even assess bacterial viability. Machine learning has further enhanced feature extraction and classification accuracy, and THz-



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based methods have shown notable advantages in multi-class microbial identification, detection of antibiotic-resistant strains, and quantitative analysis of microbial concentrations. However, current THz technologies are still constrained by strong water absorption, limited penetration depth, and the lack of standardized spectral databases. Future efforts should focus on mitigating water background interference, improving detection in complex samples, and establishing unified microbial spectral standards. This review systematically summarizes the latest advances of THz technologies in microbial detection, analyzes their mechanisms, advantages, and translational challenges, and proposes directions for future research.

【Key words】 terahertz spectroscopy; microorganisms; terahertz time-domain spectroscopy; terahertz near-field imaging; thermal curve; metamaterials; imaging; machine learning; microbial detection

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微生物与人类健康关系密切,微生物群落失衡是众多感染性疾病的关键病因^[1-2]。在口腔领域表现为龋病^[3]、牙周病^[4]及口腔黏膜病^[5]等,其发生与发展均与特定微生物菌群的定植、代谢及宿主免疫应答密切相关^[6]。龋病主要由变异链球菌等致龋菌代谢产酸,导致牙体硬组织脱矿^[7-8];牙周病则是由牙龈卟啉单胞菌^[9]、具核梭杆菌^[10]等病原体引发,造成牙周支持组织的慢性炎症破坏^[11-12];此外,白念珠菌等机会致病菌的感染还可能引起口腔黏膜疾病及全身性播散风险^[13-14]。研究表明,口腔菌群失衡甚至会加剧肠道细菌的异位定植,影响肝胆、肠道等全身健康^[15-17]。因此,对病原微生物进行精准、高效的检测与鉴定,是实现相关疾病早诊早治及有效预防的基石。

现行的微生物检测技术主要涵盖基于培养的形态学与生化鉴定、分子生物学检测及免疫学分析三大类^[18-19]。其中,培养法存在周期长^[20]、通量低及对难培养微生物检出率有限等固有局限^[21];聚合酶链式反应(polymerase chain reaction, PCR)及其衍生技术的检测性能依赖于引物设计的准确性,且操作流程易受污染干扰,成本较为高昂^[22-23];基于抗原-抗体反应的免疫学方法(如酶联免疫法)则受制于抗体亲和力与特异性的制约,在区分近缘菌种方面存在不足^[24-25]。上述这些传统检测方法虽在特异性和准确性上有一定优势,但普遍存在检测周期长、操作流程复杂等问题,且对实验条件依赖性强。这些局限性限制了即时诊断与高通量筛查的临床应用^[26-27]。

近年来,光谱技术凭借其无需标记、检测速度

快、非破坏性强等特性,逐渐在微生物检测领域展现出重要应用潜力^[28]。太赫兹(terahertz, THz)波(频率范围为0.1~10 THz)技术作为一种新兴的光谱探测手段,凭借其光子能量低、无损检测的特性^[29-30],以及能灵敏捕捉生物大分子(包括核酸^[31]、蛋白质^[32-33]、细胞膜^[34]等)“指纹”光谱的独特优势,为微生物检测提供了全新的解决方案^[35]。其中THz时域光谱技术能够通过检测微生物分子水平的结构特征和水分分布状态,实现对不同微生物(细菌、酵母菌、革兰氏阳/阴性细菌等)的区分^[36];THz近场成像凭借其纳米级空间分辨率,可实现对微生物单细胞的形态观察乃至胞外基质分布的可视化分析^[37];THz热曲线通过分析菌群随温度变化的整体介电响应,从而实现革兰氏阳/阴性细菌的微生物分类^[38];THz超材料传感技术通过电磁场局域增强机制,不仅实现了对微生物的痕量检测与精准鉴别,更通过与微流控、信号放大策略的集成,推动了多功能一体化检测平台的发展^[39]。此外,机器学习算法的引入可通过智能解析THz高维复杂的数据,从而实现了对微生物精准、高效的自动化鉴别^[40];与核酸扩增等分子生物学技术的融合,将后者卓越的特异性识别能力与THz自身的无标记、无损检测优势相结合,为实现超高灵敏度的生物传感提供了全新的技术路径^[41]。

本文旨在系统综述THz光谱技术在微生物检测中的最新研究进展,深入探讨其作用机理、技术优势与当前存在的挑战,以期为推动该技术在微生物诊断领域的深入发展与临床应用提供学术参考。

1 THz 波的物理特性与微生物检测原理

THz 波位于电磁波谱中微波与红外光之间,频率范围为 0.1~10 THz(波长 30 μm 至 3 mm),具有低光子能量(0.4~40 meV)及良好的穿透性,尤其对非极性材料如塑料、纸张和干燥的生物组织具有

较强的穿透能力^[42-44]。与红外光、微波和 X 射线等生物检测技术相比,THz 波有较高的频谱分辨率,同时低光子能量能避免电离辐射带来的生物损伤^[45-46],且相对于传统的微生物检测技术具有其独特的优势(表 1)。

表 1 太赫兹光谱与传统微生物检测技术的对比总结

Table 1 Comparison between terahertz spectroscopy and conventional microbial detection techniques

Method	Applications	Advantages	Limitations
Terahertz	Rapid screening	Non-destructive	Water interference
Culture + Biochemical identification	Clinical diagnosis and antimicrobial testing	Low cost, viable isolates obtainable	Slow, culture-dependent
Serology	Clinical screening and epidemiological surveys	Simple and rapid	Limited specificity
PCR/qPCR	Pathogen detection and quantification	High sensitivity, quantitative	High cost, requires DNA extraction
16S rRNA sequencing	Community analysis and bacterial identification	High-throughput, culture-independent	High cost
Fluorescence in situ hybridization	Spatial distribution of microbes	Visualization, in situ localization	Complex probe design

PCR: polymerase chain reaction

THz 波检测微生物的原理在于生物细胞内的生物大分子(如蛋白质、脂质、多糖)及水分子在 THz 频段具有独特的电磁响应。不同种类微生物因其细胞壁结构和分子组成差异,会在 THz 光谱中形成类似“指纹”的特征图谱^[47-48]。其物理基础主要包括:①生物大分子的低频振动与弛豫(即“松弛”,指体系在受到外界电场扰动后逐渐恢复到平衡状态的过程)。这些分子运动会消耗 THz 波能量并改变其传播速度,从而在 THz 光谱中留下峰值或位移信号^[49-50];②水分子对 THz 波的吸收和折射。自由水分子能够快速运动,而紧贴在细胞壁或大分子表面的“结合水”运动受限。水分子之间的氢键稳定性和翻转速度差异,会在 THz 波段产生吸收和折射率的变化^[51];③局域电场效应和“界面极化”。在细胞膜和细胞外基质等界面区域,局部电荷分布不均会导致局域电场增强或削弱,即局域电场效应,进而引发“界面极化”现象,即分子在电场作用下发生重新排列,这种效应会进一步影响 THz 波的吸收强度和共振位置^[52]。THz 光谱能够将这些大分子振动、水分子效应及界面极化等微观机制映射为宏观可见的光谱特征,为临床微生物的无损鉴定提供新的技术路径^[53]。

2 THz 光谱在微生物检测中的应用

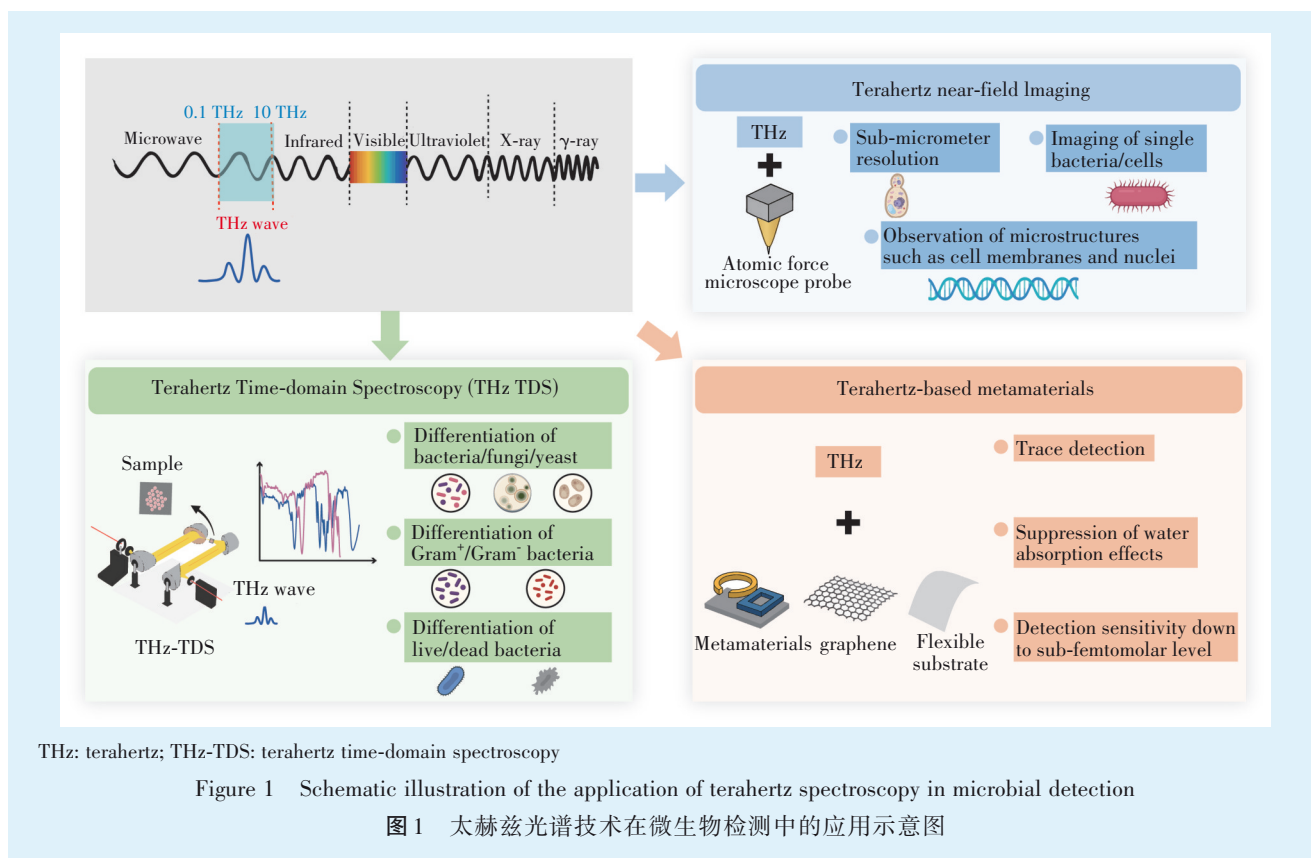
基于检测原理和应用场景的差异,THz 光谱技

术主要聚焦于基于 THz 时域光谱的微生物指纹识别技术^[54]、突破衍射极限的 THz 近场显微成像技术^[55]、具有信号增强特性的 THz 超材料传感器^[39]及结合人工智能算法^[56]的智能光谱分析系统几个方面,推动了细菌识别、活性状态评估和环境与临床样本检测等多层次研究的开展(图 1)。

2.1 基于 THz 时域光谱的微生物识别技术

THz 时域光谱(terahertz time-domain spectroscopy, THz-TDS)技术通过发射亚皮秒级超短 THz 脉冲的 THz 波,并测量这些波与微生物相互作用后的变化,经傅里叶变换转化为可分析的光谱数据,从而测定样品的折射率和吸收系数^[51, 57]。这项技术的突出特点在于:能够直接检测微生物内部蛋白质^[58]、核酸^[49]等重要成分的独特振动特征,且避免核酸提取和扩增步骤,适合临床快速原位鉴定;对微生物内部水分含量及其分布状态变化非常敏感;且整个检测过程无需任何化学标记或复杂的前期处理步骤。Tang 等^[59]通过 THz-TDS 结合微流控体系,证明了可对未经扩增的 DNA 寡核苷酸进行无标记、直接检测并区分单碱基突变,且对短链寡核苷酸的识别效果优于长链。

THz-TDS 技术主要通过以下三个方面的特征差异来区分不同微生物:首先,不同类型的微生物(如革兰氏阳性细菌和阴性细菌)因其细胞壁结构不同^[60],表现出独特的光谱特征^[52]。革兰氏阳性



菌和阴性菌的差异主要源于细胞膜结构。革兰氏阴性菌具有三层结构：外膜、薄肽聚糖层和胞质膜；而革兰氏阳性菌缺乏外膜，肽聚糖层厚度约30~100 nm，含有阴离子聚合物如磷酸类似物^[60]，因此通过THz检测可得到不同的吸收系数及折射率信息，从而实现区分。Yu等^[36]的研究表明THz-TDS可通过检测微生物细胞对THz波的不同响应特性，包括介电系数与吸收系数等的差异，可有效区分革兰阳性细菌、革兰阴性细菌、酵母菌、霉菌等不同微生物，且无需培养或染色步骤。其次，活菌和死菌由于细胞膜完整性和新陈代谢状态的差异，会在光谱上呈现可区分的响应；基于此特征，THz-TDS技术不仅可以鉴别细菌存活状态，且能够动态监测细胞代谢活动和细胞状态变化^[61]。第三，微生物在不同生长阶段或受到药物作用时，其内部结构的变化也会导致光谱特征的改变。这种技术为微生物的快速鉴定和活性评估提供了一种全新的检测手段^[62]。

整体而言，THz-TDS技术能够通过检测微生物分子水平的结构特征和水分分布状态，实现对微生物的高精度识别。该技术通过分析特征性的光谱吸收峰位置、信号强度变化以及频率偏移模式，

可以区分原核生物及真核生物(细菌、酵母菌、真菌)以及革兰氏阳性细菌和革兰氏阴性细菌等不同种类的微生物，并判断微生物的存活状态。最重要的是，这一检测过程无需使用荧光标记或其他化学修饰，也不会对样品造成任何损伤，充分保留了样本的原始状态和生物活性。这种非破坏性的检测特性使其特别适用于临床微生物样本的分析，为感染性疾病的快速诊断和治疗监测提供了新的技术手段。

2.2 基于THz近场成像的微生物识别技术

相较于传统THz-TDS技术，THz近场成像技术(terahertz near-field imaging)通过突破衍射极限，实现远低于波长尺度(可达亚微米级)的空间分辨率，实现了细菌、真菌单体的形态结构观察与THz介电特性检测^[63-64]。THz近场成像可分为散射型扫描近场光学显微镜(s-SNOM)和近场光电导天线两类^[65-66]，其中s-SNOM因其高空间分辨率和对样品表面局部结构的敏感性，被广泛应用于微生物形态与功能特性的研究^[63]。与其他光学成像方法相比，THz s-SNOM不仅能够实现超高空间分辨率和非侵入性检测，还可提供丰富的THz光谱信息，有助于分析微生物的成分与代谢状态^[55]。然而，

该技术仍存在信噪比有限、成像速度较慢等局限性。为提升性能,研究者通过优化探针设计(如减小探针顶端半径^[67]、增强局部电场)、引入高次谐波解调信号处理方法^[68],以及将s-SNOM与其他显微技术(如原子力显微镜)^[69]相结合等策略,显著改善了成像质量和信息获取能力,实现了对单个菌体细胞内部结构(如核质分布、细胞膜厚度)与种类判别的精准检测,在菌种识别和活性评估中表现优异^[70-71]。例如,Wang等^[72]利用THz s-SNOM成功获得大肠杆菌与金黄色葡萄球菌的超分辨近场光谱图,并通过分析两种细菌特征性的光谱信号差异实现了这两种细菌单体的区分。

在胞内组成方面,THz近场成像能够揭示微生物的内核结构^[73]、胞壁厚度与胞外多糖基质(如生物膜胞外多糖)在近场信号中的影响,推动对生物膜形成机制与菌体代谢状态的监测^[74]。Zhang等^[37]使用THz s-SNOM对口腔微生物,包括致龋微生物(变异链球菌及其突变株)、口腔常见细菌(口腔链球菌属)及真菌(白念珠菌)等不同微生物进行THz近场成像,通过双核高斯滤波器对THz近场图像进行降噪处理,并用Image-J测量可获得细菌的细胞直径及胞壁厚度等信息,并成功观察到不同菌种胞外多糖基质的独特空间排布模式。尽管目前尚缺乏针对唾液样品的系统研究,这些成果提示THz技术在口腔微生物无创成像和动态监测中具有潜力,未来研究仍需进一步验证其在高水分复杂介质中的抗干扰能力,以促进临床转化应用。

2.3 基于THz热曲线的微生物识别技术

THz超材料结合热曲线分析(THz thermal curve analysis, TTCA)被用于微生物快速鉴定,该传感平台通常由可产生共振的THz超材料结构和可控加热装置组成,将微生物样品均匀涂布在超材料表面,随着温度升高,微生物会经历生长、热灭活、DNA变性和细胞壁破坏等阶段,导致微生物的介电特性发生变化,导致超材料谐振频率偏移,从而形成特征性的热曲线,可用于微生物分类。Jun等^[38]通过热曲线的差异成功区分了细菌和酵母菌以及革兰氏阳性菌和革兰氏阴性菌,并从混合细菌中区分出了目标病原菌。随后,Jeong等^[75]将该方法扩展用于蓝藻细胞的识别。然而,基于热响应的THz方法适用于菌群样本,其空间分辨率有限,难以捕捉单个细菌尺度的形态特征。

2.4 基于THz超材料的微生物痕量检测及多功能

集成检测平台

THz超材料是一类通过人工设计的微纳结构,其核心在于在远小于波长的尺度上构造具有特殊电磁响应的单元,如分裂环谐振器、Fano共振器、类电磁感应透明结构等。①分裂环谐振器是由金属微环或微槽组成的闭合或半闭合环结构,在特定THz频率下产生强烈的电磁共振^[76];②Fano共振器是通过设计让一个离散共振模式与连续背景模式干涉,形成非对称共振峰。该峰对局域微小变化非常敏感,可显著增强弱信号检测能力^[77-78];③类电磁感应透明结构是在超材料中构建两种耦合谐振单元,使得原本吸收的频段出现透射窗口,模拟量子电磁感应透明效应。该结构可形成低损耗高灵敏响应^[79-80]。这些结构能够在特定THz频段形成强烈的局域电场信号,极大地增强与样本之间的相互作用,从而对环境中的极微小的变化产生显著响应^[81-82]。这种“放大”效应使超材料对生物样本的微小扰动高度敏感,适用于检测细胞表面的折射率变化、生物分子的吸附行为以及细胞结构的微观扰动^[83-84],形成一种多功能的痕量检测平台。

研究发现,细菌沉积在THz超材料表面时,其细胞壁结构、膜蛋白构象及局部含水率的细微差异,均可引起THz共振频率的偏移或吸收强度的变化,实现无标记、无损的快速识别^[85]。例如,当革兰氏阳性与阴性细菌分别吸附于超材料表面时,局部电磁环境被显著改变,进而表现出截然不同的THz响应特征,从而完成细菌的区分^[86-87]。

基于此,THz超材料传感技术正从单一检测向多功能集成平台快速发展。①信号放大机制提升灵敏度:在提升检测灵敏度与特异性方面,通过引入金纳米粒子、滚环扩增等信号放大机制,THz超材料的检测灵敏度已实现至亚飞摩尔级别^[31]。②微流控平台减少水分干扰:Zhao等^[88]构建了一种基于Fano共振超表面的微流控THz传感平台,对大肠杆菌和头孢氨苄的检测下限分别达 5×10^3 CFU/mL和 $5 \mu\text{g/mL}$ 。③纳米复合物与适配体增强特异性:Yu等^[86]通过结合 $\text{Fe}_3\text{O}_4@Au$ 纳米复合物与适配体功能化超材料,实现对金黄色葡萄球菌的线性响应检测,检测下限为 4.78×10^2 CFU/mL。④多谐振模式实现定量识别:Ma等^[87]基于电偶极子和环形偶极子构建的THz超材料,实现了对大肠杆菌和金黄色葡萄球菌的定量识别,最低检测下限约 10^4 CFU/mL。

这些研究表明,基于THz超材料的传感平台在微生物痕量检测和生物活性分析中具有广阔的应用前景。此外,超材料设计不断向柔性、可控方向发展,例如利用柔性PET基底、石墨烯及掺杂硅材料,可提高器件在复杂生理环境(如体液)中的稳定性,并有效抑制水分吸收带来的信号干扰^[89-91]。

2.5 THz光谱与机器学习算法的融合应用

由于THz光谱数据维度高、特征复杂,多元统计和机器学习算法被广泛应用以提升识别效率与准确率。THz光谱与机器学习算法的融合应用在微生物及生物大分子的检测中取得了显著进展^[40]。THz检测能够捕捉微生物样本中的独特频谱特征,包括细胞壁成分、膜结构以及细胞内的水分子结合状态等信息。然而,原始光谱数据通常包含高维度、多变量和复杂的噪声信号,传统分析方法难以充分挖掘数据中的深层特征和微小差异。

将支持向量机(support vector machine, SVM)、随机森林(random forest, RF)、卷积神经网络(convolutional neural network, CNN)等机器学习算法应用于THz光谱分析中,不仅提升了微生物分类准确率,还增强了对微弱特征(如特征峰偏移、吸收强度变化等)的识别能力^[36, 92]。Zhou等^[93]通过THz-s-SNOM获取金黄色葡萄球菌标准株、大肠杆菌标准株和金黄色葡萄球菌耐药株的THz近场图像,同时得到THz近场强度值及细菌高度值,然后在氨苄西林作用一小时后,比较THz近场强度曲线中同一高度值区间(40~80 nm)内的近场强度值,应用SVM算法完成大肠杆菌与金黄色葡萄球菌的区分以及金黄色葡萄球菌标准株及耐药株的区分,准确率高达90%以上。Hu等^[94]利用THz光谱结合多种机器学习算法(包括PCA-RF与CARS-RBF-SVM)对痕量黄曲霉毒素溶液进行定性识别,其中CARS-RBF-SVM模型的预测准确率高达99.17%,显示了机器学习在THz光谱高精度识别中的关键作用。此外,CNN算法在THz光谱图像识别中表现出优异的特征提取能力,能够自动捕捉谱图中的微弱变化,进一步提升检测的灵敏度和特异性^[95]。Wang等^[96]通过引入CNN,有效提升了THz混合谱(吸收率+折射率)对20种氨基酸的特征提取与分类性能,在两组测试集上实现了99.9%和99.2%的高准确率,相较仅用吸收谱提升约12.5%和23%,充分凸显了深度学习方法在THz光谱智能

识别中的优势。

2.6 THz光谱与分子生物检测技术的融合应用

目前,THz光谱技术也与聚合酶链式反应扩增技术及等温核酸检测协同应用,具有在临床诊断与现场快速检测领域扩展应用的潜力。

2.6.1 THz光谱与PCR扩增技术的融合 PCR是分子生物学中最为常用的核酸扩增技术,广泛应用于病原微生物的快速检测与鉴定,但其检测通常依赖凝胶电泳或荧光标记探针,存在操作复杂、易受污染干扰等局限^[97]。研究者尝试将PCR技术与THz-TDS技术相融合,利用THz波对极性生物大分子的敏感性,实现核酸扩增产物的无标记、非接触式检测^[98]。与直接检测微生物整体结构的方式不同,THz-TDS与核酸扩增技术结合,可以提升检测灵敏度并适用于低丰度样本。Arora等^[99]首次报道了该融合策略的可行性,研究将不同长度(133 bp与697 bp)的细菌DNA用PCR扩增后直接置于水相中,通过THz-TDS监测其在0.3~1.2 THz频段内的光谱响应,发现DNA溶液较缓冲液表现出显著的吸收增强和折射率变化,且吸收强度与DNA浓度呈正相关关系,最低检出下限可达0.1 ng/ μ L,实现了THz-TDS对水相中PCR产物的无标记识别。

2.6.2 THz光谱与等温滚环扩增技术的融合 鉴于PCR对热循环设备需求高、操作复杂,等温扩增技术也逐渐受到关注。等温滚环扩增(rolling circle amplification, RCA)无需像PCR那样进行温度循环,在等温条件下即可实现高倍率DNA扩增,更适合现场快速检测。Yang等^[41]创新性地将RCA扩增体系与THz-TDS相结合,构建了一种特异性强、无需标记的细菌DNA等温检测方法,实现了对合成DNA(下限约0.12 fmol)及基因组DNA(最低浓度约0.05 ng/ μ L)的高灵敏检测,并在干扰菌存在下维持优异特异性。

除PCR与RCA外,环介导等温扩增(loop-mediated isothermal amplification, LAMP)因其扩增效率高、设备要求低,已广泛用于现场病原体检测^[100]。若与THz光谱结合,则有望在扩增结束后直接对产物进行无标记、非接触式的光谱读取,减少对荧光探针和电泳分析的依赖。在CRISPR/Cas检测体系方面,已有研究利用THz光谱监测Cas12a剪切反应前后的频谱差异,实现了肿瘤ctDNA的高灵敏识别(下限可达0.8 fmol),显示出THz在CRISPR体系中作为信号转导方式的潜力^[101]。此

外,THz光谱也已被用于构建基于适配体(一类通过体外筛选获得的单链DNA、RNA或短肽分子,能特异性识别并结合目标分子,且合成简便、稳定性高和易于修饰)的分子特异性生物传感器,在血清样本中实现了对目标分子的灵敏、无标记检测^[89]。这些探索表明,THz光谱不仅可与核酸扩增技术协同,也具备与多种分子检测方法融合的应用前景。

3 THz技术在微生物检测中的局限性

尽管THz技术在微生物检测中具有明显优势,但其临床应用仍存在诸多挑战。微生物样品的物理和生化特性对THz响应具有高敏感性,样品厚度、密度与粗糙度直接影响THz波的穿透深度和信噪比^[102];细胞内外水分的含量及其结合状态(自由水或结合水)是决定THz吸收特性的关键因素^[51]。在实际检测中,THz波对水极其敏感,水分的强吸收会严重降低信号强度并掩盖目标光谱特征,导致检测灵敏度下降^[103],为缓解水分干扰,研究者已开发出微流控样品腔^[104]、差分谱校正^[105]及光谱去噪算法^[106]等技术,但这些方法虽能部分改善信号质量,仍难完全消除水分对检测的影响,未来仍需在样品制备、光谱校正及数据处理方法上进一步优化。其次,THz波的穿透能力有限,对于较厚或复杂的样本如混合菌群,检测效果受限,难以实现深入分析^[29],未来仍需在增强THz穿透性及信号获取方法上进一步优化。此外,尚缺乏标准化的THz频谱数据库和微生物光谱图谱,对于实际中复杂混合菌群的识别与解析仍依靠经验、算法训练,限制了技术的大规模推广和临床应用^[107],因此构建标准化数据库已成为发展趋势。

4 总结与展望

THz光谱技术在微生物检测中已形成以频谱指纹识别、近场成像增强与超材料放大为核心的多层次检测体系,并通过与智能算法和核酸扩增平台的融合,显著提升了检测效率、灵敏度与实用性,为推动微生物快速诊断、活性评估及临床样本分析提供了坚实的技术基础。THz光谱技术的临床应用仍处于初步探索阶段,面临水分吸收、穿透能力受限、缺乏标准化数据库及复杂生物样品信号稳定性等挑战。未来研究需在优化THz与多技术融合、建立覆盖不同微生物及生理状态的标准化的频谱数据库、开展多中心临床验证以及探索与其他成像或光学传感技术结合等方面展开,以推

动其从实验向临床转化,实现微生物快速检测、动态监测及个性化诊疗的应用潜力。

近年来,THz光谱技术在口腔医学领域的应用逐渐受到关注。除了检测口腔微生物,其在牙齿早期脱矿及颌面部肿瘤等方面也展现了独特潜力^[108]。THz光谱技术能够在无损、无标记条件下捕捉牙釉质和牙本质中水分及微观矿物结构变化,从而实现龋病的早期识别^[109]。THz元传感器能用于区分健康与癌变的口腔细胞^[110]。利用类电磁感应透明超材料构建的THz传感器能实现不同浓度癌细胞的检测^[111],但THz在口腔医学中的应用仍属于起步阶段,有待进一步创新与开发。

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