Advances in Analytical Chemistry 分析化学进展, 2022, 12(4), 317-326
Published Online November 2022 in Hans. http://www.hanspub.org/journal/aac
https://doi.org/10.12677/aac.2022.124038

Hans汉斯

细菌电化学检测及应用

华　宇[1]，崔海珊[1]，胡玉林[2]，刘　扬[1*]，吴增强[1*]

[1]南通大学公共卫生学院，江苏　南通
[2]南通大学化学化工学院，江苏　南通

收稿日期：2022年10月17日；录用日期：2022年11月7日；发布日期：2022年11月18日

摘　要

细菌感染是公共卫生领域面临严重挑战之一，而且由于抗生素的滥用导致的细菌耐药性的现象也越来越严重。因此发展一种快速、灵敏度高，选择性好的细菌检测方法对细菌干扰的处理具有重要意义。电化学传感器成本低廉、能耗低、易于自动化及微型化等内在优势使其具备快速、定量对细菌进行检测的优势，尤其可以通过与微流控技术、纳米技术等集成发展用于复杂样本的现场、快速及高灵敏检测。该综述主要从电化学生物传感器、微流控芯片和纳米通道等三个方面对细菌电化学检测的近年来的进展进行了系统概述。

关键词

细菌检测，电化学方法，传感器，微流控芯片，纳流控

Electrochemical-Based Detection of Bacteria

Yu Hua[1], Haishan Cui[1], Yulin Hu[2], Yang Liu[1*], Zengqiang Wu[1*]

[1]School of Public Health, Nantong University, Nantong Jiangsu
[2]School of Chemistry and Chemical Engineering, Nantong University, Nantong Jiangsu

Received: Oct. 17th, 2022; accepted: Nov. 7th, 2022; published: Nov. 18th, 2022

Abstract

Bacterial infection has been regarded as one of main challenges in public health field. However, beyond infection, antibiotic resistance of bacteria results in medical inefficiency and chronic infections due to misusing in antimicrobial drugs. Therefore, developing a bacterial identification

*通讯作者。

文章引用: 华宇, 崔海珊, 胡玉林, 刘扬, 吴增强. 细菌电化学检测及应用[J]. 分析化学进展, 2022, 12(4): 317-326.
DOI: 10.12677/aac.2022.124038

that could rapidly distinguish different bacterial species with high sensitivity and selectivity guides the treatment of bacterial infection. Electrochemical-based bacterial detection holds considerable promise for low-cost monitoring bacterial growth and analyzing bacterial species with miniaturization devices in complex samples. In this review, recent advances in electrochemical-based bacterial detections are discussed from electrochemical sensors, microfluidic method, and nanofluidic method and debated future trends of electrochemical-based methods.

Keywords

Bacteria Detection, Electrochemical Method, Sensors, Microchip, Nanofluidics

1. 引言

虽然细菌广泛存在于人体与环境之中，幸运的是，这些细菌大多对人类是无害的。甚至有许多细菌与它们的人类宿主形成了互补的有益关系。即便如此，导致人类疾病的致病菌株却也普遍存在，并对公共卫生构成了严重威胁，每年有一百多万人死于细菌感染[1] [2] [3]。尽管已经有许多方法被用于细菌检测，但这些方法仍然依赖于传统的培养技术，缺乏通用性且不适合现场监测[4] [5] [6]。因此，寻求简单、快速、便携且不受场所限制的诊断技术已成为目前细菌测试技术发展的首要目标，也是细菌检测面临的巨大挑战。随着分析检测技术的发展，电化学技术已经在细菌检测方面取得了很大的成功[7] [8] [9]。电化学检测提供了实验室分析的所有优点(特异性、选择性和灵敏度)，并具有床边检测(POC)所需的低成本和快速度的特点。从而在细菌的监测与检测方面得到广泛应用[10] [11]。在本综述中，我们主要从电化学生物传感器、微流控芯片和纳米通道等三个方面对细菌电化学检测的近年来的进展进行了系统概述和展望。

2. 基于电化学生物传感器的细菌检测

电化学生物传感器(Electrochemical Biosensors)通过电极上的生物识别分子捕获目标分析物，进而使电极表面性质发生改变而影响电极的电流、电位、阻抗信号，根据监测到的电信号的变化来定量目标分析物的浓度[12]。电化学生物传感器因其高灵敏度、低成本、快速、操作简便等特点在细菌检测方面有着极其广泛的应用[13] [14] [15] [16]。一般根据电信号响应类型，将电化学分析方法分为阻抗分析法、电流分析法和电位分析法[17]。

2.1. 阻抗分析法

阻抗技术对于电极表面性质变化的响应非常灵敏，该技术通过细菌与电极表面的识别分子之间相互作用后电极表面性质的改变来实现对细菌检测。具有不需纯化样品、无需标记物、分析快速灵敏等优点，近些年来得到了广泛应用[18] [19] [20] [21]。基于阻抗分析的原理，阻抗分析可以分为两类方法，一类是基于电极表面存在氧化还原反应的法拉第阻抗分析，另一类是基于电极表面双电层电容变化的阻抗分析。如图 1 所示，ArazNorouzDizaji 等[22]开发了一种万古霉素修饰的丝网印刷金电极(SPGEs)构成的“抗生素传感器”，用于对电化学检测全细胞形态的对万古霉素敏感的革兰氏阳性菌的特异性检测，并采用电化学阻抗谱(EIS)对金黄色葡萄球菌(*Staphylococcus aureus*)、大肠埃希菌(*Escherichia coli*)和耻垢分枝杆菌(*Mycolicibacterium smegmatis*)进行了验证。EIS 结果显示，革兰氏阳性的万古霉素敏感金黄色葡萄球菌在

SPGE-Van 平台上有很强的附着能力，而耐万古霉素大肠杆菌和耻垢分枝杆菌(分别为革兰氏阴性菌和耐酸菌)没有明显的结合特性。然后，采用不同浓度(10~10^8 CFU/mL)的金黄色葡萄球菌来考察所提出的传感器平台的灵敏度。检测限和定量限分别为 $10^{1.58}$ 和 $10^{4.81}$ CFU/mL。此外，Jiao [23]课题组制作了一种阻抗生物传感器用于检测腹泻样品中的空肠弯曲杆菌，该方法分析患者粪便样本中的空肠弯曲杆菌的细菌水平与 PCR 检测结果能较好的吻合，极大地提升了检测速度。

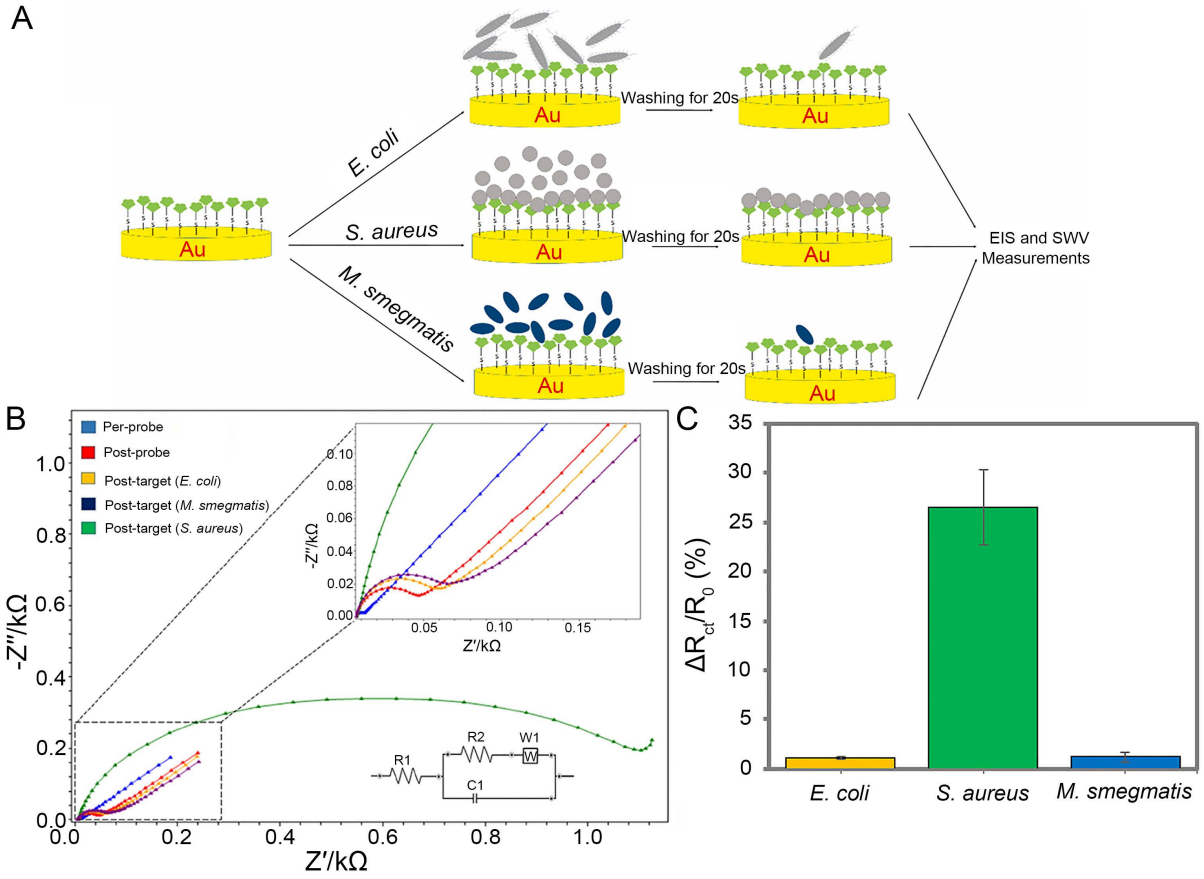

Figure 1. (A) Schematic illustration of the interaction between SPGE-Van with different bacteria. (B) Representative EIS spectrums related to different bacteria and the Randles equivalent circuit used for data fitting. (C) Rct signal changes according to the bacteria. Reprinted with permission from ref [22]. Copyright 2021 Clearance Center

图 1. (A) SPGE-Van 与不同细菌相互作用的示意图。(B) 不同细菌的代表性 EIS 谱及兰德尔等效电路进行数据拟合。(C) 不同细菌的 Rct 信号图[22]

2.2. 电流分析法

电流型的传感器类似于一个电解槽。电流型生物传感器主要检测不同物质浓度下氧化还原反应引起的电流变化，其电极的输出信号与被测物浓度呈线性关系[21] [24] [25] [26]。如图 2 所示，由于大肠杆菌与电极表面的碰撞导致铁氰化钾扩散到电极表面受阻，进而造成电流下降，使微电极上检测到溶液中的单个大肠杆菌，同时电流下降的频率可以用于测量细菌的浓度[27]。Jiang 等[28]开发一种基于丝网印刷技术的一次性电极，用差分脉冲伏安法记录受革兰氏阴性菌外壁脂多糖(LPS)影响的电流信号。结果表明，肠道沙门氏菌血清型肠炎的 LPS 使峰值电流显著增加，该方法的检出限为 3.5×10^{-3} ng/mL，线性检测范围为 1×10^{-2}~3 ng/mL。目前，电流型传感器最大的挑战是干扰问题，及其它离子对目标检测物质的干扰，因此需要在未来做进一步改善。

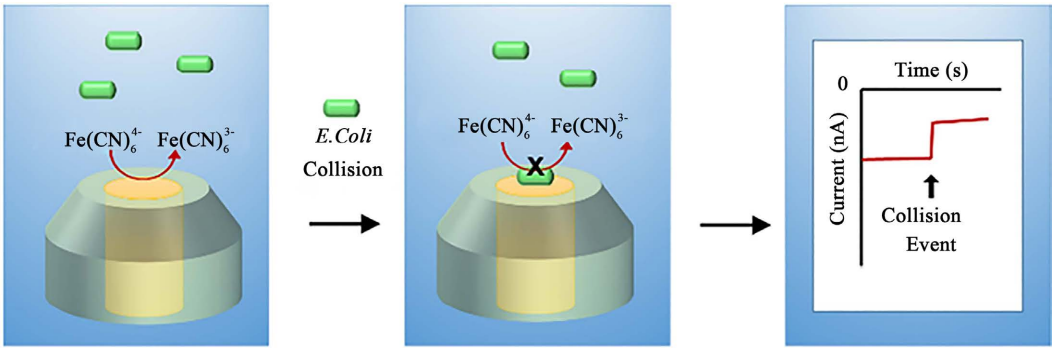

Figure 2. Schematic diagram of *E. coli* detection by collision event on ultramicroelectrode (UME). Reprinted with permission from ref [27]. Copyright 2018 Clearance Center
图 2. 基于超微电(UME)碰撞事件检测大肠杆菌的示意图[27]

2.3. 电位分析法

基于测量电位变化的分析方法称为电位计量法。电位测量系统由一个在一定温度下电极电位恒定的参比电极和一个电位随分析物浓度变化的指示电极组成。电位传感器具有快速、便携、经济、灵敏度高、操作方便、设备简单等优点[29] [30] [31]。如图 3 所示，Enguang [32]报告了一种一次性聚合膜丝网印刷电极(SPE)，利用抗菌肽的固有电荷和其独特的识别能力，避免了探针标记和指示物的添加，细菌与抗菌肽的结合可以有效地阻止肽被萃取到掺杂离子交换剂的聚合物膜中，从而产生电位变化。该工作以对金黄色葡萄球菌的检测水平可达 10 CFU/ml。

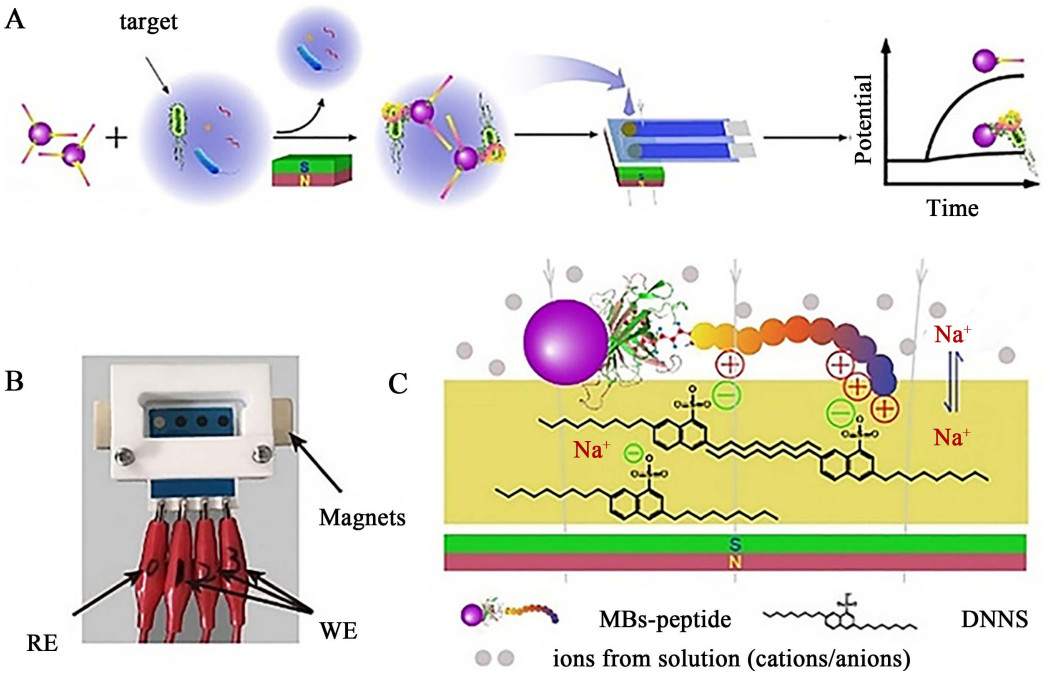

Figure 3. (A) Illustration of the potentiometric assay for bacterial cells based on the MBs-peptide. (B) Photograph of the setup for potentiometric detection. The screen-printed electrodes include working electrodes (WE, acting as indicator electrodes for the potentiometric assay) and a reference electrode (RE). (C) Illustration of the response mechanism of MB-peptide on the polymeric membrane ion-sensitive. Reprinted with permission from ref. [32]. Copyright 2021 Clearance Center
图 3. (A) 基于 MBs-肽的细菌细胞电位测定原理图[32]。(B) 电位检测装置照片。丝网印刷电极包括工作电极(WE，作为电位测定的指示电极)和参比电极(RE)。(C) MB 肽在聚合物膜离子敏感电极上的响应机理

3. 基于微流控芯片的细菌检测

近些年来，微流控芯片技术(Microchip)以其便携性、小型化、自动化、高通量检测、节约成本等优点成为细菌检测应用的强大助手[33] [34] [35]。与传统方法相比，微流控的最大优势是其构建过程与待测物所处微环境相似，可精确驱动和控制微通道中的待测物，提高检测灵敏度[36]。另外，样品预处理、反应、分离和检测，都可集成到单个微流控芯片中，适用于现场测试应用[33]。同时，其它技术与微流控芯片相结合，可用于食源性病原体的检测[37] [38]。现在，一些新颖的微流控芯片已经成功地用于细菌检测。例如，基于微流控的电化学系统的 DNA 传感器的开发，用于沙门氏菌检测[39]；基于免疫磁性纳米颗粒与脲酶结合，采用电化学阻抗快速检测大肠杆菌的微流控平台[40]；以及将电化学阻抗与交错电极阵列(IDE 阵列)结合，用于检测火鸡肉里沙门氏菌的微流控平台[41]。如图 4 所示，通过制备微流控生物传感器[42]，采用磁分离、酶催化和电信号分离检测鼠伤寒沙门菌(*Salmonella typhimurium*)。将生物亲和素修饰的磁性纳米颗粒(MNPs)通过亲和素－生物素系统与抗沙门氏菌的生物素化单克隆抗体(MABs)结合形成免疫 MNPs，最终沙门氏菌与 MNPs 形成免疫结合体，再利用磁场分离的方法从样品中分离出 MNP－细菌复合物(磁性细菌)。

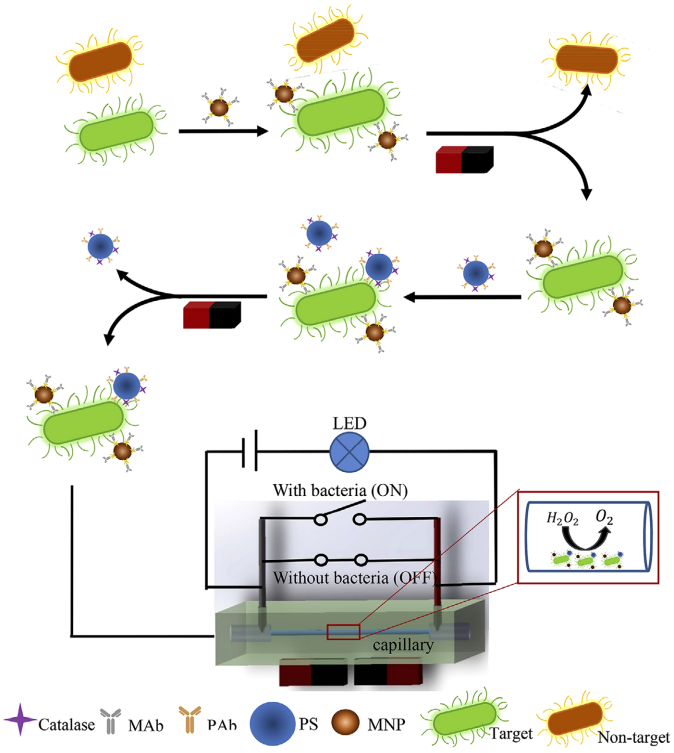

Figure 4. The principle of the proposed biosensor based on immunomagnetic separation, enzymatic catalysis and electrical signal-off for detection of Salmonella typhimurium. Reprinted with permission from ref. [42]. Copyright 2019 Clearance Center
图 4. 基于免疫磁分离、酶催化和电信号关闭的鼠伤寒沙门菌生物传感器的原理[42]

然后，利用抗沙门氏菌多克隆抗体(PAbs)和过氧化氢酶修饰的聚苯乙烯微球(PSs)与磁性细菌反应形成 MNP－细菌－PS－过氧化氢酶复合物(酶细菌)，并将其注入微流控芯片的毛细管中，通过高梯度磁场捕获。最后，在毛细管内注入过氧化氢，在酶细菌上的过氧化氢酶催化下产生氧气，在毛细管内形成气隙，从而使施加在毛细管上的电信号发生变化，并通过测量电压变化来确定目标细菌的浓度。在最佳条件下，该传感器能够在 2 h 内检测出低至 33 CFU/mL 的伤寒沙门氏菌。此外，Dastider 等人[43]提出了一种微流控传感器用于检测鼠伤寒沙门氏菌，该传感器采用高密度叉指电极阵列检测微流控芯片内的沙门氏菌细胞，将单

克隆抗沙门菌抗体固定在电极阵列表面，从而提高检测鼠伤寒沙门菌的特异性，并用阻抗分析仪测量并记录传感器的响应信号。该生物传感器能够在 3 小时内完成定性和定量分析，无需任何富集步骤。然而，基于微流控的细菌检测方法仍然具有挑战性[44]。例如，在微流控通道中，微流控传感器在达到小体积的样品所要求的灵敏度、选择性和稳定性方面可能会遇到障碍。此外，在微流控芯片上整合有效的生物识别分子具有挑战性[45] [46]。

4. 基于纳米通道的细菌检测

纳米孔道可以分为纳米孔(nanopore)和纳米通道(nanochannel)两种。纳米孔一般是指孔径在 1~100 nm，并且孔径大于其自身长度的孔道，而对于孔的长度远大于孔径的孔道，一般称为纳米通道。一方面，纳米通道具有检测特异性与信号放大功能；另一方面，纳米通道尺寸灵活性且具有强大的化学和机械性能。利用纳米通道的优异的传输特性，且与电化学相结合后还具有简便快速、信号灵敏、环保且价格低廉等优点，其成为细菌检测的强大工具[47] [48] [49]。Escosura-Muñiz 等[50]提出了一种利用纳米多孔氧化铝膜电流监测金黄色葡萄球菌分泌的毒力因子透明质酸酶(HYAL) (如图 5)。该方法基于抗体-HYAL 免疫复合物形成后会阻断纳米通道，从而引起的电流发生改变进行监测，检测限低至 64 UI/mL (17.3 U/mg) HYAL。此外，Yi 等[51]提出了一种具有自清洁特性的纳米多孔水凝胶，无需任何样品预处理，可以在全

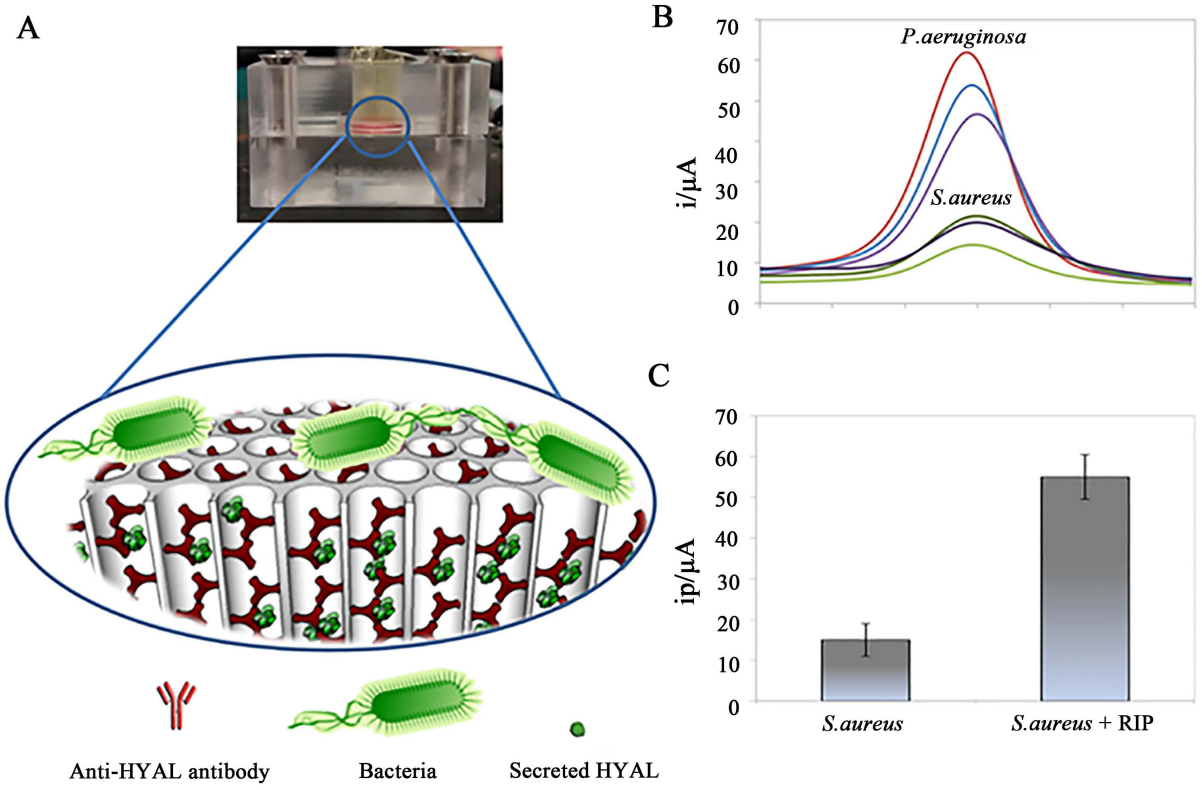

Figure 5. (A) Scheme illustrating the bacteria culture on the nanoporous membranes and the continuous capturing of secreted HYAL by the antibodies inside the nanochannels. (B) Voltammograms corresponding to three different cultures of *P. aeruginosa* and of *S. aureus*. Bacterial concentration at OD_{600} = 0.1. Incubation time: 24 h. (C) Analytical signals obtained for *S. aureus* cultures before and after treatment with anti-infective RNAIII-inhibiting peptide (RIP, YSPWTNF-NH2). Reprinted with permission from ref. [50]. Copyright 2019 American Chemical Society

图 5. (A) 细菌在纳米多孔膜上的培养和纳米通道内的抗体连续捕获分泌的 HYAL 的装置原理图。(B) 对应铜绿假单胞菌和金黄色葡萄球菌三种不同培养物的伏安图。细菌浓度在 OD_{600} = 0.1。孵育时间 24 h。(C) 抗感染抑制肽(RIP, YSPWTNF-NH2)治疗前后金黄色葡萄球菌培养物的分析信号[50]

血中直接等温扩增，进行单个细菌的计数。Luis Pla 等[52]提出了一种基于适配体门控纳米材料的高选择性平台，用于特异性金黄色葡萄球菌的检测。此外，纳米孔与宏基因组测序[53]相结合，使细菌下呼吸道感染的快速临床诊断成为可能，并可能有助于减少广谱抗生素的使用。对于复杂微生物群落，其细菌组成一般依靠因美纳(Illumina)公司的基因测序仪器确定，纳米孔测序技术在检测鼻菌群细菌时可以媲美 Illumina 基因测序[54]，为复杂微生物群落的细菌检测提供了新方法。

尽管基于纳米通道的细菌检测已经取得了重大进展，但仍有一些问题需要解决。例如，修饰后的纳米通道性能并不总是非常稳定，精确控制纳米通道上有效修饰的比例仍然是一项艰巨的任务。另外，在高离子强度下，纳米通道的检测能力因双电层厚度减小而下降的问题仍需要解决。

5. 结论

综上所述，基于电化学原理的细菌检测方法具有高灵敏度、快速的优点，已经实现对单个细菌以及其代谢过程的电化学检测。而且，电化学检测易于微型化便于携带，非常适合于一些医疗资源匮乏的地区对细菌干扰的快速、低成本的检测，从而避免造成由于检测延误产生的重大公共卫生事件。但是，如何提高电化学检测方法的特异性以及解决电极表面的生物污染对检测信号的干扰是当前该方法实现商业化应用必须考虑的问题。

致　谢

感谢国家自然科学基金面上项目(21974058, 21775066)资助。感谢南通大学高层次人才科研启动经费的资助。

基金项目

国家自然科学基金面上项目(21974058, 21775066)资助。

参考文献

[1] Scallan, E., Hoekstra, R.M., Angulo, F.J., Tauxe, R.V., Widdowson, M.A., Roy, S.L., Jones, J.L. and Griffin, P.M. (2011) Foodborne Illness Acquired in the United States—Major Pathogens. *Emerging Infectious Diseases*, **17**, 7-15. https://doi.org/10.3201/eid1701.P11101

[2] Low, N. and Broutet, N.J. (2017) Sexually Transmitted Infections—Research Priorities for New Challenges. *PLOS Medicine*, **14**, e1002481. https://doi.org/10.1371/journal.pmed.1002481

[3] Wi, T.E., Lahra, M., Ndowa, F.J., Bala, M., Dillon, J.R., Ramón-Pardo, P., Eremin, S.R., Bolan, G.A. and Unemo, M. (2017) Antimicrobial Resistance in *Neisseria gonorrhoeae*: Global Surveillance and a Call for International Collaborative Action. *PLoS Medicine*, **14**, e1002344. https://doi.org/10.1371/journal.pmed.1002344

[4] Lazcka, O., Del Campo, F.J. and Muñoz, F.X. (2007) Pathogen Detection: A Perspective of Traditional Methods and Biosensors. *Biosensors & Bioelectronics*, **22**, 1205-1217. https://doi.org/10.1016/j.bios.2006.06.036

[5] Swaminathan, B. and Feng, P. (1994) Rapid Detection of Food-Borne Pathogenic Bacteria. *Annual Review of Microbiology*, **48**, 401-426. https://doi.org/10.1146/annurev.mi.48.100194.002153

[6] Paniel, N., Baudart, J., Hayat, A. and Barthelmebs, L. (2013) Aptasensor and Genosensor Methods for Detection of Microbes in Real World Samples. *Methods* (*San Diego, Calif.*), **64**, 229-240. https://doi.org/10.1016/j.ymeth.2013.07.001

[7] McEachern, F., Harvey, E. and Merle, G. (2020) Emerging Technologies for the Electrochemical Detection of Bacteria. *Biotechnology Journal*, **15**, e2000140. https://doi.org/10.1002/biot.202000140

[8] Simoska, O. and Stevenson, K.J. (2019) Electrochemical Sensors for Rapid Diagnosis of Pathogens in Real Time. *The Analyst*, **144**, 6461-6478. https://doi.org/10.1039/C9AN01747J

[9] Amiri, M., Bezaatpour, A., Jafari, H., Boukherroub, R. and Szunerits, S. (2018) Electrochemical Methodologies for the Detection of Pathogens. *ACS Sensors*, **3**, 1069-1086. https://doi.org/10.1021/acssensors.8b00239

[10] Ivnitski, D., Abdel-Hamid, I., Atanasov, P., Wilkins, E. and Stricker, S. (2000) Application of Electrochemical Bio-

sensors for Detection of Food Pathogenic Bacteria. *Electroanalysis*, **12**, 317-325. https://doi.org/10.1002/(SICI)1521-4109(20000301)12:5<317::AID-ELAN317>3.0.CO;2-A

[11] Monzó, J., Insua, I., Fernandez-Trillo, F. and Rodriguez, P. (2015) Fundamentals, Achievements and Challenges in the Electrochemical Sensing of Pathogens. *The Analyst*, **140**, 7116-7128. https://doi.org/10.1039/C5AN01330E

[12] Ronkainen, N.J., Halsall, H.B. and Heineman, W.R. (2010) Electrochemical Biosensors. *Chemical Society Reviews*, **39**, 1747-1763. https://doi.org/10.1039/b714449k

[13] Nakamura, H. and Karube, I. (2003) Current Research Activity in Biosensors. *Analytical and Bioanalytical Chemistry*, **377**, 446-468. https://doi.org/10.1007/s00216-003-1947-5

[14] Farooq, U., Ullah, M.W., Yang, Q., Aziz, A., Xu, J., Zhou, L. and Wang, S. (2020) High-Density Phage Particles Immobilization in Surface-Modified Bacterial Cellulose for Ultra-Sensitive and Selective Electrochemical Detection of *Staphylococcus aureus*. *Biosensors & Bioelectronics*, **157**, Article ID: 112163. https://doi.org/10.1016/j.bios.2020.112163

[15] Neufeld, T., Schwartz-Mittelmann, A., Biran, D., Ron, E.Z. and Rishpon, J. (2003) Combined Phage Typing and Amperometric Detection of Released Enzymatic Activity for the Specific Identification and Quantification of Bacteria. *Analytical Chemistry*, **75**, 580-585. https://doi.org/10.1021/ac026083e

[16] Yang, L. and Bashir, R. (2008) Electrical/Electrochemical Impedance for Rapid Detection of Foodborne Pathogenic Bacteria. *Biotechnology Advances*, **26**, 135-150. https://doi.org/10.1016/j.biotechadv.2007.10.003

[17] Naresh, V. and Lee, N. (2021) A Review on Biosensors and Recent Development of Nanostructured Materials-Enabled Biosensors. *Sensors* (*Basel*, *Switzerland*), **21**, Article No. 1109. https://doi.org/10.3390/s21041109

[18] Samanta, N., Kundu, O. and Chaudhuri, C.R. (2013) A Simple Low Power Electronic Readout for Rapid Bacteria Detection with Impedance Biosensor. *IEEE Sensors Journal*, **13**, 4716-4724. https://doi.org/10.1109/JSEN.2013.2272522

[19] Wang, Y., Ye, Z. and Ying, Y. (2012) New Trends in Impedimetric Biosensors for the Detection of Foodborne Pathogenic Bacteria. *Sensors* (*Basel*, *Switzerland*), **12**, 3449-3471. https://doi.org/10.3390/s120303449

[20] Wan, Y., Zhang, D. and Hou, B. (2009) Monitoring Microbial Populations of Sulfate-Reducing Bacteria Using an Impedimetric Immunosensor Based on Agglutination Assay. *Talanta*, **80**, 218-223. https://doi.org/10.1016/j.talanta.2009.06.057

[21] Furst, A.L. and Francis, M.B. (2019) Impedance-Based Detection of Bacteria. *Chemical Reviews*, **119**, 700-726. https://doi.org/10.1021/acs.chemrev.8b00381

[22] NorouzDizaji, A., Ali, Z., Ghorbanpoor, H., Ozturk, Y., Akcakoca, I., Avci, H. and Dogan Guzel, F. (2021) Electrochemical-Based "Antibiot Sensor" for the Whole-Cell Detection of the Vancomycin-Susceptible Bacteria. *Talanta*, **234**, Article ID: 122695. https://doi.org/10.1016/j.talanta.2021.122695

[23] Huang, J., Yang, G., Meng, W., Wu, L., Zhu, A. and Jiao, X. (2010) An Electrochemical Impedimetric Immunosensor for Label-Free Detection of *Campylobacter jejuni* in Diarrhea Patients' Stool Based on O-carboxymethylchitosan Surface Modified Fe_3O_4 Nanoparticles. *Biosensors & Bioelectronics*, **25**, 1204-1211. https://doi.org/10.1016/j.bios.2009.10.036

[24] McEachern, F., Harvey, E. and Merle, G. (2020) Emerging Technologies for the Electrochemical Detection of Bacteria. *Biotechnology Journal*, **15**, e2000140. https://doi.org/10.1002/biot.202000140

[25] Chaubey, A. and Malhotra, B.D. (2002) Mediated Biosensors. *Biosensors & Bioelectronics*, **17**, 441-456. https://doi.org/10.1016/S0956-5663(01)00313-X

[26] Grieshaber, D., MacKenzie, R., Vörös, J. and Reimhult, E. (2008) Electrochemical Biosensors—Sensor Principles and Architectures. *Sensors* (*Basel*, *Switzerland*), **8**, 1400-1458. https://doi.org/10.3390/s80314000

[27] Kuss, S., Amin, H. and Compton, R.G. (2018) Electrochemical Detection of Pathogenic Bacteria-Recent Strategies, Advances and Challenges. *Chemistry*, *an Asian Journal*, **13**, 2758-2769. https://doi.org/10.1002/asia.201800798

[28] Jiang, H., Yang, J., Wan, K., Jiang, D. and Jin, C. (2020) Miniaturized Paper-Supported 3D Cell-Based Electrochemical Sensor for Bacterial Lipopolysaccharide Detection. *ACS Sensors*, **5**, 1325-1335. https://doi.org/10.1021/acssensors.9b02508

[29] Isildak, Ö. and Özbek, O. (2020) Silver(I)-Selective PVC Membrane Potentiometric Sensor Based on 5,10,15,20-tetra (4-pyridyl)-21H, 23H-porphine and Potentiometric Applications. *Journal of Chemical Sciences*, **132**, Article No. 29. https://doi.org/10.1007/s12039-019-1734-2

[30] Isildak, Ö., Özbek, O. and Gürdere, M.B. (2020) Development of Chromium(III)-Selective Potentiometric Sensor by Using Synthesized Pyrazole Derivative as an Ionophore in PVC Matrix and Its Applications. *Journal of Analysis and Testing*, **4**, 273-280. https://doi.org/10.1007/s41664-020-00147-8

[31] Singh, A.K., Mehtab, S. and Saxena, P. (2006) A Bromide Selective Polymeric Membrane Electrode Based on Zn(II) Macrocyclic Complex. *Talanta*, **69**, 1143-1148. https://doi.org/10.1016/j.talanta.2005.12.028

[32] Lv, E., Li, Y., Ding, J. and Qin, W. (2021) Magnetic-Field-Driven Extraction of Bioreceptors into Polymeric Membranes for Label-Free Potentiometric Biosensing. *Angewandte Chemie* (*International ed.*), **60**, 2609-2613. (In English) https://doi.org/10.1002/anie.202011331

[33] Zhao, X., Li, M. and Liu, Y. (2019) Microfluidic-Based Approaches for Foodborne Pathogen Detection. *Micro-Organisms*, **7**, Article No. 381. https://doi.org/10.3390/microorganisms7100381

[34] Zhou, L., Chen, Y., Fang, X., Liu, Y., Du, M., Lu, X., Li, Q., Sun, Y., Ma, J. and Lan, T. (2020) Microfluidic-RT-LAMP Chip for the Point-of-Care Detection of Emerging and Re-Emerging Enteric Coronaviruses in Swine. *Analytica Chimica Acta*, **1125**, 57-65. https://doi.org/10.1016/j.aca.2020.05.034

[35] Gao, Y.F., Pan, X.X., Xu, S., Liu, Z.J., Wang, J.S., Yu, K.Z., Wang, C.F., Yuan, H.C. and Wu, S. (2020) Fluorescence-Enhanced Microfluidic Sensor for Highly Sensitive *In-Situ* Detection of Copper Ions in Lubricating Oil. *Materials & Design*, **191**, Article ID: 108693. https://doi.org/10.1016/j.matdes.2020.108693

[36] Nasseri, B., Soleimani, N., Rabiee, N., Kalbasi, A., Karimi, M. and Hamblin, M.R. (2018) Point-of-Care Microfluidic Devices for Pathogen Detection. *Biosensors & Bioelectronics*, **117**, 112-128. https://doi.org/10.1016/j.bios.2018.05.050

[37] Chen, Q., Wang, D., Cai, G., Xiong, Y., Li, Y., Wang, M., Huo, H. and Lin, J. (2016) Fast and Sensitive Detection of Foodborne Pathogen Using Electrochemical Impedance Analysis, Urease Catalysis and Microfluidics. *Biosensors & Bioelectronics*, **86**, 770-776. https://doi.org/10.1016/j.bios.2016.07.071

[38] Mašková, T., Hárendarčíková, L. and Petr, J. (2017) Determination of *Escherichia coli* in Urine Using a Low-Cost Foil-Based Microfluidic Device. *Talanta*, **170**, 36-40. https://doi.org/10.1016/j.talanta.2017.03.089

[39] Savas, S., Ersoy, A., Gulmez, Y., Kilic, S., Levent, B. and Altintas, Z. (2018) Nanoparticle Enhanced Antibody and DNA Biosensors for Sensitive Detection of Salmonella. *Materials* (*Basel, Switzerland*), **11**, Article No. 1541. https://doi.org/10.3390/ma11091541

[40] Yao, L., Wang, L., Huang, F., Cai, G., Xinge, X. and Lin, J. (2018) A Microfluidic Impedance Biosensor Based on Immunomagnetic Separation and Urease Catalysis for Continuous-Flow Detection of *E. coli* O157:H7. *Sensors and Actuators B—Chemical*, **259**, 1013-1021. https://doi.org/10.1016/j.snb.2017.12.110

[41] Liu, J., Jasim, I., Shen, Z., Zhao, L., Dweik, M., Zhang, S. and Almasri, M. (2019) A Microfluidic Based Biosensor for Rapid Detection of Salmonella in Food Products. *PLOS ONE*, **14**, e0216873. https://doi.org/10.1371/journal.pone.0216873

[42] Hou, Y., Cai, G., Zheng, L. and Lin, J. (2019) A Microfluidic Signal-Off Biosensor for Rapid and Sensitive Detection of Salmonella Using Magnetic Separation and Enzymatic Catalysis. *Food Control*, **103**, 186-193. https://doi.org/10.1016/j.foodcont.2019.04.008

[43] Dastider, S.G., Barizuddin, S., Yuksek, N.S., Dweik, M. and Almasri, M.F. (2015) Efficient and Rapid Detection of Salmonella Using Microfluidic Impedance Based Sensing. *Journal of Sensors*, **2015**, Article ID: 293461. https://doi.org/10.1155/2015/293461

[44] Zhang, D., Bi, H., Liu, B. and Qiao, L. (2018) Detection of Pathogenic Microorganisms by Microfluidics Based Analytical Methods. *Analytical Chemistry*, **90**, 5512-5520. https://doi.org/10.1021/acs.analchem.8b00399

[45] Foudeh, A.M., FatanatDidar, T., Veres, T. and Tabrizian, M. (2012) Microfluidic Designs and Techniques Using Lab-on-a-Chip Devices for Pathogen Detection for Point-of-Care Diagnostics. *Lab on a Chip*, **12**, 3249-3266. https://doi.org/10.1039/c2lc40630f

[46] Jiang, Y., Zou, S. and Cao, X. (2016) Rapid and Ultra-Sensitive Detection of Foodborne Pathogens by Using Miniaturized Microfluidic Devices: A Review. *Analytical Methods*, **8**, 6668-6681. https://doi.org/10.1039/C6AY01512C

[47] Ding, D., Gao, P., Ma, Q., Wang, D. and Xia, F. (2019) Biomolecule-Functionalized Solid-State Ion Nanochannels/Nanopores: Features and Techniques. *Small* (*Weinheim an der Bergstrasse, Germany*), **15**, e1804878. https://doi.org/10.1002/smll.201804878

[48] Ali, M., Yameen, B., Cervera, J., Ramírez, P., Neumann, R., Ensinger, W., Knoll, W. and Azzaroni, O. (2010) Layer-by-Layer Assembly of Polyelectrolytes into Ionic Current Rectifying Solid-State Nanopores: Insights from Theory and Experiment. *Journal of the American Chemical Society*, **132**, 8338-8348. https://doi.org/10.1021/ja101014y

[49] Li, X., Zhai, T., Gao, P., Cheng, H., Hou, R., Lou, X. and Xia, F. (2018) Role of Outer Surface Probes for Regulating Ion Gating of Nanochannels. *Nature Communications*, **9**, Article No. 40. https://doi.org/10.1038/s41467-017-02447-7

[50] Escosura-Muñiz, A., Ivanova, K. and Tzanov, T. (2019) Electrical Evaluation of Bacterial Virulence Factors Using Nanopores. *ACS Applied Materials & Interfaces*, **11**, 13140-13146. https://doi.org/10.1021/acsami.9b02382

[51] Yi, C., Luo, Z., Lu, Y., Belwal, T., Pan, X. and Lin, X. (2021) Nanoporous Hydrogel for Direct Digital Nucleic Acid Amplification in Untreated Complex Matrices for Single Bacteria Counting. *Biosensors & Bioelectronics*, **184**, Article ID: 113199. https://doi.org/10.1016/j.bios.2021.113199

[52] Pla, L., Santiago-Felipe, S., Tormo-Más, M.Á., Pemán, J., Sancenón, F., Aznar, E. and Martínez-Máñez, R. (2020) Aptamer-Capped Nanoporous Anodic Alumina for *Staphylococcus aureus* Detection. *Sensors and Actuators B—Chemical*, **320**, Article ID: 128281. https://doi.org/10.1016/j.snb.2020.128281

[53] Charalampous, T., Kay, G.L., Richardson, H., Aydin, A., Baldan, R., Jeanes, C., Rae, D., Grundy, S., Turner, D.J., Wain, J., Leggett, R.M., Livermore, D.M. and O'Grady, J. (2019) Nanopore Metagenomics Enables Rapid Clinical Diagnosis of Bacterial Lower Respiratory Infection. *Nature Biotechnology*, **37**, 783-792. https://doi.org/10.1038/s41587-019-0156-5

[54] Heikema, A.P., Horst-Kreft, D., Boers, S.A., Jansen, R., Hiltemann, S.D., de Koning, W., Kraaij, R., de Ridder, M., van Houten, C.B., Bont, L.J., Stubbs, A.P. and Hays, J.P. (2020) Comparison of Illumina versus Nanopore 16S rRNA Gene Sequencing of the Human Nasal Microbiota. *Genes*, **11**, Article No. 1105. https://doi.org/10.3390/genes11091105