Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Elsevier hereby grants permission to make all its COVID-19-related research that is available on the COVID-19 resource centre - including this research content - immediately available in PubMed Central and other publicly funded repositories, such as the WHO COVID database with rights for unrestricted research re-use and analyses in any form or by any means with acknowledgement of the original source. These permissions are granted for free by Elsevier for as long as the COVID-19 resource centre remains active.
Electrochemiluminescence sensing platform for microorganism detection

Jun Li a, Jianliang Shen b,*, Ruogu Qi a,*

a School of Medicine & Holistic Integrative Medicine, Nanjing University of Chinese Medicine, Nanjing 210023, China
b State Key Laboratory of Ophthalmology, Optometry, and Vision Science, School of Ophthalmology and Optometry, School of Biomedical Engineering, Wenzhou Medical University, Wenzhou 325027, China

Electrochemiluminescence (ECL) is a type of luminescence in which substances produced on electrode undergoes an electron transition to an excited state for light-emitting [1]. As a sensing platform, ECL instruments have been widely used in clinical diagnosis, environmental monitoring, food and water safety, biological defense and other fields benefiting from their low detection limits, extensive dynamic range, fast detection speed, and low instrument cost. In this perspective, we highlight some representative examples of microbial detection by ECL sensing platforms in biosafety and health applications.

The first example is the ECL biosensor for diagnosing COVID-19 which caused the global pandemic. Zhang et al. established an ECL platform driven by entropy to detect the RdRp-COVID, an important target of SARS-CoV-2, which was used to diagnose the COVID-19 [2] (Table 1). Instead of represented assay which applied recombinant protein representing the nucleocapsid (N) antigen for the determination of antibodies against SARS-CoV-2 such as Electrocsys® Anti-SARS-CoV-2, this ECL biosensor contains gold electrode modified DNA tetrahedron (D.T.) and Ru bipyridine (bpy)3+ modified S3 DNA probe. In the presence of the target DNA, the Ru (bpy)3+ modified S3 DNA probe was ligated to the linear ssDNA capture probe in the D.T., amplified reaction of target DNA in the electrode surface had occurred through the entropy-driven method, and eventually generated the signal, which was described as an “ECL on” state. Moreover, D.T. was used for the scaffold on the gold electrode and promoted the even distribution, and reduced the hybridization reactions of single-stranded DNA. Thus, the amplification reaction did not require an enzyme, which reduced the cost of mass screening of SARS-CoV-2 patients. This ECL biosensor had already done the detection of RdRp-COVID in human serum samples spiked with target DNA with both high specificity and sensitivity, which relatively reached a limit of detection (LOD) down (2.67 FM), compared with the colorimetric (0.038 nM) and fluorescence (81 pM).

Meanwhile, Hua Tang et al. designed the ECL biosensing method to detect group B streptococci (GBS) [3] (Table 1). This ECL biosensing strategy consists of CuMn-CeO2 loading PEI-luminal complex and multi-component DNAzyme (MNAzyme) as GBS-recycling amplification. In their study, PEI was applied as a co-reactant that enhanced the luminophore efficiency through intramolecular interaction, and CuMn-CeO2 provided a large specific surface area and promoted the capability oxidation of H2O2 (co-reactant) through high catalytic performance to achieve ultra-sensitivity of ECL signals. The MNAzyme system was used to specifically detect the target through circulation and amplification for a nucleic acid sequence of GBS. Notably, this ECL biosensing method was directly applied to test GBS with 51 pregnant women through vaginal/anal swabs in a clinic. Compared with traditional PCR method based on fluorescence, the ECL biosensing exhibited similar accuracy, including clinical vaginal/anal swab detection specificity and sensitivity.

Furthermore, it simplified the cascade signal amplification procedures by excluding complex biological enzymes and precision instruments. Thus, this research explored a practical application for the clinical diagnosis of bacteria. ECL was also used to kill pathogenic bacteria through produced reactive oxygen species (ROS) mediated by an activated photosensitizer, which was applied as ECL-therapeutics [4].

Another example of ECL biosensor is used for antimicrobial susceptibility testing (AST), effective technology for guiding antibiotic prescription by testing the antibiotic’s sensitivity to bacteria. Fen Ma et al. designed the ECL biosensor comprised NH2-MIL-53(Al) electrode for bacterial detection [5] (Table 1). This ECL biosensor contains ruthenium complex tagged concanavalin A (Ru-Con A) as ECL probe and ruthenium (II) complex (Ru) as ECL-emitting material. In the presence of E. coli BL21, Ru-Con A specifically recognized the LPS secreted by E. coli BL21 and formed the LPS-Con A conjugate, subsequently emitting the ECL signal. After treating with different antibiotics such as β-lactams (cefpiorlo group (CPO), imipenem (IPM), non-β lactams (tetracycline (TCY) and levofloxacin hydrochloride (LVX)), they found that ECL signals varied depending on the number of LPS-Con A conjugates affected by different antibiotics. Therefore, the type of clinical antibiotic and the bacterial strain being processed can be determined according to this sensor’s degree of ECL signal, which provides a simple solution for clinical antibiotic stewardship. The ECL biosensor used as antimicrobial susceptibility testing also was applied to evaluate the selectivity for the other types of bacteria such as Enterococcus faecalis, streptococcus mutants, staphylococcus aureus, and salmonella pullorum. However, the results showed no significant change for the ECL signal. Moreover, we summarized some representative studies...
for ECL strategies in an application, probe, and characteristic are in Table 1.

### Summary and perspectives

The ECL-based platform combines different identification sensors and has diversified application prospects due to the low detection limit, high specificity, fast detection speed, diversified detection targets, and portable instrument. For example, the Elesys®, an ECL platform developed by Roche, was authorized by Food and Drug Administration to screen SARS-CoV-2 infection against the current worldwide pandemic, which shows that the ECL platform has established itself as a powerful tool for ultrasensitive detection of a wide range of microorganisms. However, it is still urgent to develop novel detection methods with high sensitivity, sufficient specificity, and simple instrument requirements due to the limits of sensitive detection of samples in complex environments. Therefore, new ECL sensing systems, such as aggregation-induced emission-based ECL (AIE-ECL), upconversion nanoparticles (UCNPs), hydrophilic luminol derivative, nanomaterial, and near-infrared (NIR) ECL as optimized emitters, inorganic and organic compound and nanomaterials (N.M.s) as efficient co-reaction accelerator (CRA), and stainless steel, very-high-density electrochemical sensing, and electrodes decorated by conductive polymer hydrogels (CPHs) and nanomaterial as new electrodes platform will be investigated and fully applied [11,12]. Moreover, there are growing interests in the co-detection of multiple microorganisms with high specificity and sensitivity, such as immune sensors, adaptation sensors, gene sensors, and cell sensors [13].

Furthermore, based on the characteristics of the detected substance such as electron transfer sensitivity, ECL detection platforms without a specific sensor will be designed [7]. The broad clinical requirements of the ECL sensing platform in microbial detection will facilitate new analytical applications, such as food safety, water safety, and environmental monitoring applications. Future research should develop portable, intelligent, low-cost, highly stable, high-specific, environmentally friendly ECL platforms, which may better solve various uncertain crises.

### Acknowledgements

This work was supported by the Zhejiang Provincial Natural Science Foundation of China (LZ19H180001) and Jiangsu Specially-Appointed Professor Talent Program.

### Conflict of interest statement

The authors declare that there are no conflicts of interest.

### Author contributions

Jin Li: Writing – Original Draft. Jianliang Shen: Writing – Review & Editing. Ruogu Qi: Writing – Review & Editing.

### References

[1] M.M. Richter, Electrochemiluminescence (ECL), Chem. Rev. 104 (6) (2004) 3003–3036, https://doi.org/10.1021/cr020373d.

[2] Z. Fan, B. Yao, Y. Ding, J. Zhao, M. Xie, K. Zhang, Entropy-driven amplified electrochemiluminescence biosensor for RdRp gene of SARS-CoV-2 detection with self-assembled DNA tetrahedron scaffolds, Biosens. Bioelectron. 178 (2021), 113015. https://doi.org/10.1016/j.bios.2021.113015.

[3] J. Ling, M. Zhao, F. Chen, X. Zhou, X. Li, S. Ding, H. Tang, An enzyme-free electrochemiluminescence biosensor for ultrasensitive assay of Group B Streptococcus based on self-enhanced luminol complex functionalized CuMn-CoO2 nanospheres, Biosens. Bioelectron. 127 (2019) 167–173, https://dx.doi.org/10.1016/j.bios.2018.12.012.

[4] S. Liu, H. Yuan, H. Bai, P. Zhang, F. Lv, L. Liu, Z. Dai, J. Rao, S. Wang, Electrochemiluminescence for electric-driven antibacterial therapeutics, J. Am. Chem. Soc. 140 (6) (2018) 2284–2291, https://dx.doi.org/10.1021/jacs.7b12140.

[5] L. Sun, Y. Chen, Y. Duan, F. Ma, Electrogenated chemiluminescence biosensor based on functionalized two-dimensional metal-organic frameworks for bacterial detection and antimicrobial susceptibility assays, ACS Appl. Mater. Interfaces. 13 (32) (2021) 38923–38930, https://dx.doi.org/10.1021/acsami.1c11949.

[6] Y. He, Y. Liu, L. Cheng, Y. Yang, B. Qiu, L. Guo, Y. Wang, Z. Lin, G. Hong, Highly reproducible and sensitive electrochemiluminescence biosensors for HPV detection based on bovine serum albumin carrier platforms and hyperbranched rolling circle amplification, ACS Appl. Mater. Interfaces. 13 (1) (2021) 298–305, https://dx.doi.org/10.1021/acsami.1c02074.

[7] L.X. You, N.J. Chen, L. Wang, J. Chen, S.F. Qin, C. Rensing, Z.Y. Lin, S.G. Zhou, Electrochemiluminescence for the identification of electrochemically active bacteria, Biosens. Bioelectron. 137 (2019) 222–228, https://dx.doi.org/10.1016/j.bios.2019.04.062.

[8] N. Hao, X. Zhang, Z. Zhou, R. Hua, Y. Zhang, Q. Liu, J. Qian, H. Li, K. Wang, AgBr nanoparticles/3D nitrogen-doped graphene hydrogel for fabricating all-solid-state luminol-electrochemiluminescence Escherichia Coli aptasensors, Biosens. Bioelectron. 97 (2017) 377–383, https://dx.doi.org/10.1016/j.bios.2017.06.025.

[9] D. Feng, X. Tan, Y. Wu, C. Ai, Y. Lai, Q. Chen, H. Han, Electrochemiluminescence nanogears aptasensor based on MIL-53(Fe)(CN)3S for multiplexed detection of kanamycin and neomycin, Biosens. Bioelectron. 129 (2019) 100–106, https://dx.doi.org/10.1016/j.bios.2018.12.050.

[10] B. Babamiri, R. Hallaj, A. Salimi, Ultrasensitive electrochemiluminescence immunoassay for simultaneous determination of CA125 and CA15-3 tumor markers based on PAMAM-sulfonic acid-Ru(bpy)3(2+), and PAMAM-CdTe@CdS nanocomposite, Biosens. Bioelectron. 99 (2018) 353–360, https://dx.doi.org/10.1016/j.bios.2017.07.062.

[11] H. Wang, Advances in electrochemiluminescence co-reaction accelerator and its analytical applications, Anal. Bioanal. Chem. 413(16) (2021) 4119–4135, https://dx.doi.org/10.1007/s00216-021-03247-1.
[12] C. Ma, Y. Cao, X. Gou, J.J. Zhu, Recent progress in electrochemiluminescence sensing and imaging, Anal. Chem. 92 (1) (2020) 431–454, https://doi.org/10.1021/acs.analchem.9b04947.

[13] B. Babamiri, D. Bahari, A. Salimi, Highly sensitive bioaffinity electrochemiluminescence sensors: recent advances and future directions, Biosens. Bioelectron. 142 (2019), 111530. https://doi.org/10.1016/j.bios.2019.111530.