

# Nanotechnology in Bioanalytical Chemistry

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With the increasing advances in bioanalytical chemistry, nanotechnology has become an important tool and key technology for improving the understanding of fundamental chemistry and biology fields. The ratio of surface area to volume of materials exponentially increases at the nanoscale, leading to the emergence of numerous novel physical and chemical phenomena. For instance, the surface energy of nanomaterials becomes significantly more pronounced compared to volume energy, resulting in heightened chemical reactivity and biocompatibility of nanoparticles. When nanomaterials range in size from a few to several tens of nanometers, the motion of their electrons becomes constrained by quantum confinement effects, leading to the discretization of electron energy levels and the appearance of quantum tunneling effects. Additionally, atoms or molecules within nanostructures exhibit localized characteristics at the nanoscale, causing their physical and chemical properties to manifest significantly different optical, electrical, and magnetic properties compared to their macroscopic counterparts. In the field of bioanalytical chemistry, which is dedicated to exploring the essence of life phenomena and studying the composition, structure, function, and interactions of molecules both within and outside living organisms, nanotechnology is gradually altering our understanding of bioanalytical chemistry with its unique advantages, providing vast opportunities for scientific research and technological innovation.

The goal of this special issue is to bring together the pioneers who exploring innovative analytical techniques and advanced analytical tools aimed at enhancing sensitivity and efficiency by using nanoscience and nanotechnology and highlight their recent advances in bioanalytical chemistry. This special issue comprises 8 reviews, 9 original research articles, and 1 letter. The initial section offers a comprehensive overview of nanotechnology and its applications within the realm of

bioanalytical chemistry. This encompasses a range of nanomaterials, nanoprobe, nanofluorophores, and DNA nanodevices, along with their diverse applications in imaging, exosome analysis, molecular diagnostics, biosensing, tumor therapy, and beyond. Tan *et al.* have provided a comprehensive summary of recent advancements in specific aptamer selection for membrane proteins, aptamer-based static and dynamic membrane protein analysis, and aptamer-based molecular diagnostic techniques. Additionally, they have discussed the prospects and challenges in these fields, offering insights into the future development of these methodologies (<https://doi.org/10.1007/s40242-024-4008-6>). Nie *et al.* have summarized the current state of DNA nanodevices in biosensing and membrane anchoring mechanisms, emphasizing their applications in studying key cell membrane events, such as membrane lipid dynamics, transmembrane transport, receptor dimerization, and signal transduction. Additionally, they have discussed the challenges and potential future applications of DNA nanodevices in advancing cell membrane biology research and biomedical applications (<https://doi.org/10.1007/s40242-024-4032-6>). Pang *et al.* have summarized the recent advancements in the characterization and computation specific to ligands for quantum dots (QDs), as well as the design strategies influencing the optical properties of QDs. Furthermore, they have provided examples of the application of responsive QDs, engineered through ligand design, in sensing (<https://doi.org/10.1007/s40242-024-4034-4>). Tang *et al.* have provided a comprehensive summary of the progress made in the development of fluorescent probes for the detection of cysteine and cysteine oxidation mediated by intracellular reactive oxygen species. Additionally, they have critically analyzed the shortcomings of currently reported fluorescent probes and offered valuable insights for future probe design and optimization (<https://doi.org/10.1007/s40242-024-3290-7>). Yuan *et al.* summarized the recent research advances in water-soluble small-molecule NIR-II fluorophores, emphasizing their representative applications in bioimaging, including kidney dysfunction, tumor bioimaging, and bone-targeting bioimaging. Furthermore, they discussed the potential challenges and prospects of

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water-soluble small-molecule NIR-II fluorophores (<https://doi.org/10.1007/s40242-024-3264-9>). Na *et al.* have comprehensively summarized the latest research advancements in chemodynamic therapy (CDT) for anticancer treatment. Leveraging the unique characteristics of the tumor microenvironment (TME), including insufficient acidity, tumor hypoxia, low hydrogen peroxide ( $\text{H}_2\text{O}_2$ ) levels, and high glutathione (GSH) concentrations, they have designed various multifunctional nanomaterials. These nanomaterials are aimed at manipulating TME conditions, thereby providing increased opportunities to enhance the efficiency of CDT (<https://doi.org/10.1007/s40242-024-3267-6>). Wu *et al.* reviewed the principles, preparation, and applications of photochemical afterglow nanoparticles, and evaluated their performance in clinical sample testing by comparing with other nanoparticle-based methods. Finally, several issues and possible solutions of afterglow nanoparticle-based methods in biomarker determination were discussed (<https://doi.org/10.1007/s40242-024-3280-9>). Bai *et al.* have offered a comprehensive overview of the latest breakthroughs in the employment of nanomaterials as matrices for isolating exosomes and enriching their payloads, as substrates for laser desorption/ionization (LDI), and as platforms for signal readout and amplification in exosome mass spectrometry analysis. Additionally, they have delved into the forthcoming challenges and promising directions, ultimately striving to propel the advancement of exosome analysis techniques towards more accurate disease diagnosis and monitoring (<https://doi.org/10.1007/s40242-024-4004-x>).

The second original research part includes 10 advanced investigations, encompassing novel developments in nanotechnology and their wide applications in the field of bioanalytical chemistry. Zhang *et al.* have constructed a Pt/CeO<sub>2</sub> nanozyme, leveraging its stable peroxidase activity for the detection of choline and acetylcholine. The Pt/CeO<sub>2</sub> nanozyme overcame the influence of environmental conditions on peroxidase, offering promising prospects for clinical diagnostics and aiding in the early diagnosis and prevention of Alzheimer's disease (<https://doi.org/10.1007/s40242-024-3286-3>). Wang *et al.* devised a whole-cell bioluminescent probe based on wild-type bioluminescent bacterium *P. phosphoreum* for determining and imaging intracellular pH. This probe could accurately and reversibly reflect changes in intracellular pH in real-time, effectively revealing the disruption of intracellular pH homeostasis in *P. phosphoreum* under alkaline pH conditions (<https://doi.org/10.1007/s40242-023-3255-2>). Wang *et al.* have devised a dual-modal imaging probe, termed

OTIC NPs, combining near-infrared fluorescence imaging and photoacoustic imaging. Leveraging aggregation-induced emission active fluorophores, OTIC NPs exhibited significant photoacoustic signals, efficient generation of reactive oxygen species, and high photothermal conversion efficiency under near-infrared laser irradiation, enabling effective tumor ablation (<https://doi.org/10.1007/s40242-024-3256-9>). Ying *et al.* have achieved efficient detection of single glucose oxidase (GOD) molecules by finely tuning the balance of driving forces between electrophoretic force and electroosmotic flow within nanochannels. They extended the residence time of GOD to approximately 4 milliseconds and observed clear ionic current signals with a signal-to-noise ratio of 3.3 (<https://doi.org/10.1007/s40242-024-3281-8>). Zhang *et al.* have devised a portable point-of-care testing (POCT) platform for the dual-modal analysis of iodide ions ( $\text{I}^-$ ) by integrating colorimetric and photothermal thermometer techniques. POCT utilized G-quadruplex/Hemin (G4/Hemin) DNAzyme with peroxidase-like activity, capable of generating multicolor transitions upon the action of iodide ions ( $\text{I}^-$ ) along with an increase in temperature, enabling quantitative detection of  $\text{I}^-$  (<https://doi.org/10.1007/s40242-024-3283-6>). Xia *et al.* systematically investigated the seedless synthesis of small-sized gold nanorods (AuNRs) with diameters ranging from 5 nm to 10 nm. Their research revealed significant impacts of experimental conditions, such as the chain length of cationic surfactants, concentrations of ascorbic acid, NaBH<sub>4</sub>, and AgNO<sub>3</sub> on the resulting products. Under optimal conditions, the production yields of AuNRs with different diameters could exceed 90%, with a conversion rate of gold precursors to AuNRs ranging from 70% to 77% (<https://doi.org/10.1007/s40242-024-3289-0>). Xiao *et al.* designed a colorimetric method for the analysis of acid phosphatase (ACP) activity based on CeO<sub>2</sub>-modified gold core-shell nanoparticles (Au@CeO<sub>2</sub> NPs). By observing changes in the scattering intensity ratio of individual Au@CeO<sub>2</sub> NPs, ACP activity could be quantitatively analyzed. This method demonstrated high sensitivity and specificity, with detection limits lower than most spectroscopic measurements in bulk solution (<https://doi.org/10.1007/s40242-024-4024-6>). Chu *et al.* have designed a DNA-based artificial nanorobot. This nanorobot consisted of a DNA cube as the "body" and nucleic acid catalysts based on enzymatic nicking reactions as the "legs" for locomotion. They further devised a series of specialized tasks combining locomotion, cargo transport, and catalytic control, with real-time fluorescence kinetics curves used to monitor cargo transport and catalytic processes (<https://doi.org/10.1007/s40242-024-4025-5>). Lu *et al.* monitored the sulfur redox reaction in the presence of

oxygen-containing molecules biphenyl-4,4'-dicarboxylic acid (BDC) as electrolyte additives using *in situ* UV-visible spectroscopy. The analysis revealed the formation of [BDC-S<sub>3</sub><sup>•-</sup>] complexes through the binding of BDC with sulfur radicals, effectively inhibiting the formation of sulfur radicals and improving the capacity retention and rate capability of lithium-sulfur batteries (<https://doi.org/10.1007/s40242-024-4027-3>). Xia *et al.* innovatively coated the outer surface of nanochannels with hydrogel to form heterogeneous membranes, achieving high-sensitivity detection through specific adsorption of Cr(VI). The detection limit reached 10<sup>-11</sup> mol/L. This method provided a new choice and approach for the modification of nanochannel outer surfaces and detection platforms, with potential applications in the detection of Cr(VI) in living organisms, especially within cells (<https://doi.org/10.1007/s40242-024-4029-1>).

In summary, this special issue offers a comprehensive overview of the recent advancements in nanotechnology, encompassing innovative synthetic techniques, exceptional properties, intricate structure-function relationships, and diverse applications in bioanalytical chemistry. We look forward to this special issue providing significant platform across various sectors of the nanotechnology community within bioanalytical chemistry and facilitating the network and collaboration in related fields.

It is a great honor for us, Prof. Yuliang Zhao (Guest Editor), Prof. Chungying Chen (Guest Editor), to serve as the guest editors for this issue. Finally, we would like to thank Prof. Jihong Yu (Editor-in-Chief) and the editorial team of CRCU for their organization and support. We also thank all authors and reviewers for their contributions to this special issue.