Progress and challenges in functional nanomaterial-based suspension array technology for multiplexed biodetection

Weijie Wu | Xinyi Liu | Wanwan Li

State Key Laboratory of Metal Matrix Composites, School of Materials Science and Engineering, Shanghai Jiao Tong University, Shanghai, P. R. China

Correspondence
Wanwan Li, State Key Laboratory of Metal Matrix Composites, School of Materials Science and Engineering, Shanghai Jiao Tong University, 800 Dongchuan Road, Shanghai 200240, P. R. China.
Email: wwl@sjtu.edu.cn

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Abstract
Suspension array technology (SAT) has aroused substantial interest due to its strong multiplexed detection capability, quick binding kinetics, high throughput, and high detection sensitivity. Although rapid developments in material science have led to tremendous progress with regards to SAT, several challenges still exist that limit the performance of SAT, including limited barcode numbers, unpredictable barcode signal and suboptimal detection sensitivity. Therefore, major efforts are still needed to further improve performance to fulfill the higher requirements of precision diagnosis. In this review, we focus on summarizing recent advances regarding encoded microspheres and labels for functional nanomaterial-based suspension array technology, then analyze the current challenges and propose corresponding solutions. We anticipate that this review will be helpful for the future design of functional nanomaterial-based SAT platforms with superior performance.

KEYWORDS
encoded microspheres, functional nanomaterials, multiplexed detection, suspension array technology

INTRODUCTION
Suspension array technology (SAT) based on encoded microspheres plays a significant role in high-throughput multiplexed detection and is a powerful tool for protein profiling, gene analysis, drug discovery, disease diagnosis, and treatment monitoring as a result of quick binding kinetics, strong multiplexed detection capability, high throughput, and high detection sensitivity. SAT combines encoded microspheres and flow cytometry, such that encoded microspheres with unique signals act as carriers to identify specific analytes, after which flow cytometry is typically used as a decoding device to read both the barcode and reporter. In particular, encoded microspheres are the core technology of SAT, as they act as solid supports and allow for the identification of specific targets. Over the past two decades, tremendous progress has been made with respect to SAT, largely with the goal of improving barcode library construction, multiplexed detection capability and detection sensitivity, as well as the development of...
FIGURE 1 An encoded microspheres-based suspension array technology (SAT) bus is heading toward its destination: a detection platform with powerful multiplexed capacity and high detection sensitivity. An overview of the progress, challenges, and possible solutions of functional nanomaterial-based SAT.

wash-free platforms thanks to rapid developments in nanotechnology and material science.\(^{[6-13]}\) However, in the face of growing detection demand, especially with respect to precision diagnosis, some of SAT’s shortcomings, such as limited barcode capacity, unpredictable barcode signal, suboptimal detection sensitivity, and limited multiplexed detection capability, need to be overcome urgently.

In this review, we introduce recent progress in functional nanomaterial-based SAT for multiplexed biodetection, primarily focusing on commonly-used encoded microspheres and analyte-binding labels, which play prominent roles in SAT. Subsequently, we discuss two major challenges of SAT – limited barcoding capacity and suboptimal detection sensitivity – before giving an overview of possible solutions to these concerns (see Figure 1). This mini-review aims at providing guidance for the future development of high-performing functional nanomaterial-based SAT, especially with regards to the construction of the barcode library and increasing sensitivity, as well as to provoke broad interest in the technology’s potential applications to proteomics, genomics, drug discovery, and single-cell analysis.

2 | PROGRESS IN FUNCTIONAL NANOMATERIAL-BASED SAT FOR MULTIPLEXED BIODETECTION

2.1 | Encoded microspheres

One of the most outstanding advantages of SAT is its powerful multiplexed detection capability, which strongly depends on the number of distinguishable barcodes in one analysis. Consequently, a sufficient number of distinct barcodes is required in order to realize high-throughput multiplexed detection in SAT platforms. In order to expand the coding capacity for the construction of massive barcode libraries, many efforts have been made over the previous two decades.\(^{[6,8,10,11,14-19]}\) An ideal barcode system must fulfill the following requirements: powerful coding capacity, flexible encoding, and decoding, controllable design of coded signal, good stability, absence of signal interference between barcode and reporter, weak background noise, abundance of functional groups on the barcode surface, and proper density and diameter, among others.\(^{[1]}\) In this section, we provide an overview of several commonly used encoded microspheres (see Figure 2), including fluorescence-encoded microspheres, fluorescence lifetime-encoded microspheres, Raman-encoded microspheres, and structure color-encoded microspheres and make a comparison of their corresponding functional materials for barcoding (see Table 1).

2.1.1 | Fluorescence-encoded microspheres

Due to its powerful coding capacity, flexible encoding, high speed, and convenient decoding, the most prevalent optical coding strategies typically combine color and intensity, in contrast to encoding methods like chemical encoding, physical encoding, graphical encoding, and electronic encoding.\(^{[1,7]}\) At present, common fluorophores for optical barcodes include organic dyes, quantum dots (QDs), upconversion nanoparticles (UCNPs), and
aggregation-induced emission luminogens (AIEgens), among others. While organic dyes are currently the most common fluorophores used in commercial suspension array platforms from Luminex and BD, they present some disadvantages, including poor photostability, unavoidable cross-talk, and a need for multiple excitation lasers to excite multicolor dyes.\cite{20,21} Since Nie et al. proposed the concept of QDs barcodes in 2001, empowered by the unique optical properties of QDs, this strategy has attracted much attention and has become the most

### FIGURE 2

Several encoded microspheres commonly used in suspension array technology (SAT).\cite{6,8,19,42}

### TABLE 1

A comparison of common functional materials used for barcoding.\cite{1,2,6-8,32,43}

| Encoding materials | Encoding signal | Encoding capacity | Advantages | Disadvantages |
|--------------------|-----------------|-------------------|------------|---------------|
| Organic dyes       | Fluorescence    | +++               | Easy for encoding and decoding | Poor stability, multiple excitations, energy transfer |
| QDs                | Fluorescence and Lifetime | ++++             | Single excitation, narrow emission spectra, easy for encoding and decoding | Energy transfer |
| UCNPs              | Fluorescence and Lifetime | ++              | Low background interference | Multicolor emission, relatively low QY |
| AIEgens            | Fluorescence    | +++               | High brightness, strong fluorescence stability | Broad FWHM |
| Raman molecules    | Raman           | ++++              | Narrow spectrum, good stability, low background interference | Low decoding speed, spectral tailing |
| PhCs               | Structure color | ++                | Low background interference, large surface area, good stability | Limited barcoding capacity, difficult to achieve high-throughput |

Abbreviations: FWHM, full width at half maximum; PhC, photonic crystal; QY, quantum yield.
extensively studied approach for generating various kinds of optical barcodes.\[8–11,13–16,22,23\] Although QDs have many excellent optical properties and act as perfect candidates for coding, the major challenge of QDs-encoded microspheres is the existence of energy transfer that results from the spectral overlap between multicolor QDs, which gives rise to unpredictable barcode signal and reduces coding capacity.\[1,6,8,11,24\]

The novel fluorophores AIEgens are not emissive when molecularly dissolved but are highly emissive in the aggregated state, attracting significant interest from scientists in various research fields.\[25\] AIEgens are not only characterized by high brightness, strong photobleaching resistance, superior biocompatibility, and low background interference but also avoid the aggregation-caused quenching effect, making them an excellent choice for optical encoding.\[12,26–31\] For the first time, we established a 2D AIEgens barcode library containing 30 distinct barcodes by varying the color and intensity levels of AIEgens, showcasing high brightness and the presence of small and concentrated clusters in comparison with QDs-encoded microspheres.\[12\] More importantly, AIEgens barcodes possess excellent fluorescence stability compared with other optical barcodes reported previously. However, the broad full width at half maximum (FWHM) of AIEgens limits their coding ability compared to QDs. Therefore, further development of AIEgens with narrow FWHMs will unlock the hidden potential of optical barcodes with superior performance capabilities.

2.1.2 Fluorescence lifetime-encoded microspheres

Fluorescence lifetime is a coding element that is independent of color and intensity. Moreover, lifetime has good stability because it is an intrinsic parameter of materials. In other words, it is insensitive to variations in the concentration of fluorophores or excitation light intensity. Importantly, coding with fluorescence lifetime is an effective way to reduce background interference. UCNPs are one kind of common fluorophores with a long, adjustable lifetime (in the microsecond to millisecond range), and they can be manipulated through the doping of different lanthanides or by manipulations of the core/shell structure. More than 10 distinct lifetime-encoded microspheres were generated in a single color band by Jin and coworkers, and these could be decoded using a time-resolved confocal scanning microscope and time-resolved scanning cytometry.\[17,32\] This finding established the foundation for future construction of libraries containing more than 10,000 distinct barcodes (through combinations of color, intensity, and lifetime), breaking down the barriers of fluorescence-encoded microspheres with regards to the development of a high-capacity multiplexing platform. Zhang et al. established a matrix of binary-encoded (wavelength and lifetime) microspheres by incorporating UCNPs into porous polystyrene (PS) microspheres, demonstrating strong coding capacity (>10^5), three-order magnitudes higher than that of conventional color/intensity strategies.\[19\] However, UCNPs usually possess relatively low quantum yield (QY), leading to reduction in coding capacity when barcodes are produced in combination with photoluminescence intensity.

2.1.3 Raman-encoded microspheres

Raman dyes are another promising coding element due to their narrow spectra, strong coding capacity, good photostability, high resolution, and compatibility with a wide range of excitation lasers, from visible light to near-infrared.\[1,2,33\] Min et al. synthesized 20 polyynes with distinct Raman frequencies of narrow linewidth (13/cm), termed as the carbow, through the engineering of bond-selective isotope doping, conjugation length, and capping substitution.\[6\] In principle, 3^{10–1} = 59,048 distinguishable barcodes could be yielded by the use of ten resolvable frequencies at three intensity levels, three orders of magnitudes higher than that of common optical barcodes based on color/intensity. Nevertheless, Raman scattering is a relatively weak optical process that provides information about the unique vibrational modes of molecules.\[34\] Fortunately, surface-enhanced Raman scattering (SERS), resulting from interactions between molecules and plasmon of the metal surfaces, remarkably enhances Raman signal by factors of 10^{13–10^{14}} and has great potential to expand coding capacity.\[33–35\] However, the tailing phenomenon observed among different Raman molecules gives rise to serious signal interference and weakens encoding capacity.\[1\] Therefore, it is urgent to develop non-tailing Raman dyes with strong signal Raman molecules for use in Raman barcodes, which would improve their coding ability, reduce interference between coding and detection signals, and support the development of wide clinical applications.

2.1.4 Structure color-encoded microspheres

Structure color-encoded microspheres are synthesized on the basis of photonic crystal (PhC) materials, which are encoded according to the reflection peak of periodic nanostructures. PhCs are periodically structured dielectric materials with a photonic bandgap, which generate structure colors deriving from the light reflection of specific
frequencies.\cite{36–38} PhCs have many superior optical properties relevant to their application as structure color barcodes, including excellent stability, narrow spectral width, and reduced background signal.\cite{39–42} Moreover, SAT platforms based on structure color-encoded microspheres are usually characterized by high detection sensitivity due to the large surface area. Zhao et al. presented a PhC barcode consisting of hollow colloidal nanospheres that were assembled through microfluidic droplet templates.\cite{43}

Compared to solid PhC barcodes, these barcodes exhibited increased refractive index contrast, low density, and good suspension capacity. Nevertheless, the number of PhC barcodes is limited by its 1D coding. To expand the coding capacity of PhC barcodes, it is essential to develop new composite coding strategies that combine other encoding methods. In addition, the size of PhC barcodes is usually larger than 100 $\mu m$, which would present a challenge for the development of a high-density multiplexing platform.

### 2.2 Labels

In SAT platforms, labels acting as reporters are coupled with analytes. These labels are used to determine the concentration of analytes and greatly impact detection sensitivity. Therefore, it is essential to employ tags with high intensity and low background interference in order to achieve high detection sensitivity.

#### 2.2.1 Fluorophores

At present, fluorescence intensity is the most commonly used detection signal in SAT, and many efforts have been made to develop novel fluorophores with the superior optical performance. The most widely-used reporters in SAT platforms are traditional organic dyes, such as fluorescein isothiocyanate, R-phycoerythrin (PE), cyanine 3, and allophycocyanin, which suffer from relatively broad emission spectra, low QY, strong photobleaching, poor stability, and optical crosstalk between barcodes and reporters.\cite{12}

During the past 20 years, considerable progress has been made with respect to QDs, while issues of hydrophobicity, surface modification, and poor photostability in water have hampered their practical applications to in vitro labeling in diagnostic fields.\cite{44,45} Although UCNPs provide low background interference, they have not yet been used as labels in SAT platforms because of their multicolor emission properties and relatively low QY. In particular, AIEgens possess many excellent optical properties and have great potential as labels.\cite{27,28} A variety of novel AIEgens-based sensors have been recently developed.\cite{46–48} AIEgens nanobeads were used as labels in the SAT platform, which enhanced detection sensitivity compared to multiplex assays that used a commercial organic dye (PE) or QDs nanobeads as fluorescent signal reporters.\cite{12} Therefore, to obtain high detection performance, additional fluorophores with superior properties (such as high brightness, low background noise, and narrow FWHM) need to be developed in the future.\cite{1,49}

#### 2.2.2 SERS dots

SERS is an ultrasensitive spectroscopic technology that can support single-molecule detection in some cases; thanks to strong signal enhancement capabilities resulting from the enhanced electromagnetic fields of the plasmonic nanostructures.\cite{50–52} In addition, Raman signals also possess strong stability, narrow spectra, low background noise, the ability to be excited by a single laser, lack of photobleaching, and so forth. Therefore, SERS dots are an ideal candidate for use as nanotags to label analytes in Raman-encoded microspheres-based SAT platforms. As discussed earlier, the main challenge of SERS dots is signal interference between barcodes and reporters due to the tailing phenomenon of Raman molecules.

### 3 CHALLENGES IN FUNCTIONAL NANOMATERIAL-BASED SAT FOR MULTIPLEXED BIODETECTION

Although many efforts have been devoted to improving the performance of encoded microsphere-based SAT platforms in recent years, the achievement of stronger multiplexed detection capacity and higher detection sensitivity still faces some intractable challenges. Here, we focus on discussing the following core issues: the expansion of encoding capacity and the improvement of detection sensitivity, and further analyze possible solutions.

#### 3.1 Improving barcoding capacity

Accordingly, the achievement of high-throughput multiplexed detection in an SAT platform requires a sufficient number of distinguishable barcodes. Currently, fluorescent coding strategies that combine color and intensity are the most widely-used strategies in both scientific research and clinical diagnostics. However, the main challenge of optical barcodes is the further improvement of encoding capacity. Theoretical coding numbers of fluorescent microspheres can be calculated according to the following formula: $C = N^m - 1$, where $C$ is the number of barcodes, $m$ is the number of colors and $N$ is the number of intensity
levels. Coding capacity is greatly limited by the number of colors of fluorescent materials that can be encoded simultaneously (or the number of detection channels of flow cytometry), which causes an exponential increase in barcode number. Consequently, it is important to generate large barcode libraries by employing fluorophores with narrow FWHMs. Moreover, the spectral overlap between different fluorophores is inevitable, resulting in energy transfer between multicolor barcodes, further reducing the coding area of the fluorescence barcoding map and resulting in unpredictable barcode signals. Therefore, it is crucial to eliminate energy transfer in multicolor barcodes or to develop composite coding modes that can expand the coding capacity of widely used barcodes based on color/intensity to break the multiplexing ceiling.

### 3.1.1 Eliminating energy transfer in multicolor barcodes

Energy transfer occurs between multicolor barcodes and leads to decreased photoluminescence intensity of fluorophores emitting at shorter wavelengths while increasing the intensity of fluorophores with longer emissions, ultimately reducing the coding area of the fluorescence barcoding map and limiting coding capacity. Energy transfer, especially Förster resonance energy transfer, is a strongly distance-dependent optical phenomenon observed within a donor-acceptor pair whose components are within about 1–10 nm of each other and in which spectral overlap exists between the donor emission spectrum and the acceptor absorbance spectrum.\(^{[11,53–55]}\) In principle, two alternative routes towards eliminating energy transfer between multicolor barcodes will be reviewed: (1) regulating the distance between fluorophores of different colors and (2) eliminating spectral overlap between multicolor fluorophores.

The efficiency of energy transfer is negatively correlated to the sixth power of the distance between donor and acceptor molecules.\(^{[53,55,56]}\) When this distance is larger than the Förster distance (\(R_0\)), energy transfer can be eliminated. Hence, many chemical or physical methods have been developed to control the distance between fluorophores of different colors.\(^{[16,57,58]}\) The groups of both Xu and coworkers\(^{[57]}\) and Xu and coworkers\(^{[16]}\) doped single-color fluorophores into microspheres, then produced barcodes by mixing or conjugating beads of different colors together such as to avoid energy transfer between multicolor fluorophores. Even though these solutions allowed for accurate barcode design, they gave rise to a cumbersome fabrication process and generated complicated microspheres structures. One additional solution for eliminating energy transfer is to avoid spectral overlap; the effectiveness and simplicity of this strategy have been demonstrated.\(^{[11]}\) The key factor to avoid spectral overlap is to utilize fluorophores with large Stokes shifts. We prepared multicolor QDs barcodes and inhibited the spectral overlap among QDs of different colors by utilizing tetrapod CdSe/CdS QDs with large Stokes shift (\(\sim 180\) nm), which efficiently eliminated energy transfer and showed powerful barcoding capacity.\(^{[11]}\) An ideal set of 144 distinguishable barcodes was generated, representing the largest barcode library of QDs-encoded microspheres to date. However, the emission range of QDs with heterostructures is limited in the orange-to-red region, which would relatively limit coding capacity for multicolor encoded microspheres. Given the limitations of QDs with heterostructures in multicolor barcodes, it is important to develop new fluorophores with large Stokes shifts and wide emission regions.

### 3.1.2 Composite encoding strategy

Although fluorescence-encoding strategies allow great coding capacity, coding numbers will dramatically increase when combined with other coding strategies such as lifetime or physical elements. Our research group devoted significant attention to generating barcodes through forward scatter-color-intensity approach. The diameter of microspheres can be easily identified based on the forward scattering signal in flow cytometry. Due to the feasibility of using the Shirasu porous glass membrane emulsification method to control the size of microspheres, the approach provides great convenience for the generation of unique barcodes by combining forward scatter, color, and intensity. A 3D barcode library containing 144 distinguishable barcodes was constructed by combining three different diameters (7, 11, and 16 \(\mu\)m) and two QDs colors (green and red) at seven intensity levels, demonstrating the strong coding capacity of this encoding strategy.\(^{[11]}\) Zhang and coworkers reported a 2D coding mode that combines luminescence color with the decay lifetime of UCNPs and exhibits high barcode capacity.\(^{[19]}\) UCNPs with blue, green, and red emission were manipulated through the design of core/multi-shell structures and a controlled energy relay method, such that each color of UCNPs could easily achieve six lifetime populations. This coding strategy based on color-lifetime showed exponentially scalable encoding capacity (>100,000), which has three orders of magnitude improvement compared with that of conventional color-intensity approaches.

Overall, to enable the construction of huge barcode libraries and realize powerful multiplexed assay capacity, one effective strategy is to increase the number of barcodes by combining multiple coding methods. Moreover, with rapid developments in science and technology, it is
necessary to develop novel encoding strategies on the basis of new decoding equipment technology and materials with unique properties for the further development of SAT.

3.2  |  Improving detection sensitivity

High sensitivity is one of the advantages of SAT, due to quick binding kinetics and the large surface area of encoded microspheres. However, higher detection requirements for SAT platforms must be fulfilled with respect to samples with ultralow concentrations, including miRNA, ctDNA, and CTCs. To achieve higher detection sensitivity for SAT, three alternative routes will be reviewed: labels with high brightness, signal amplification methods, and background interference reduction.

3.2.1  |  Labels with high brightness

The optical properties of the reporter have a great influence on detection performance, especially with respect to the detection sensitivity of SAT.\cite{1} To obtain high detection sensitivity, fluorophores with high QY, low background interference, good photostability, and high labeling efficiency are typically selected for use as reporters.\cite{1,59} Thanks to tremendous progress in material science, many novel fluorophores with excellent optical performance have been developed, including QDs, AIEgens, and carbon dots. Particularly, AIEgens with excellent optical performance represent a good candidate for use as fluorescent reporters.\cite{27,28} However, some issues persist with respect to constructing a highly sensitive SAT platform using AIEgens as reporters, including their relative wide FWHM, surface modifications, and so forth.

3.2.2  |  Signal amplification

Furthermore, a powerful tool for obtaining high detection sensitivity with SAT is the amplification of fluorescence signals, which can be achieved through particle-based signal amplification and metal-enhanced fluorescence (MEF).\cite{1,60} Particle-based signal amplification refers to the integration of as many fluorophore units as possible into one particle, such that they act in an ensemble to label each binding event.\cite{12,59,61} Ultimately, this means that the detection signal is amplified and enhanced effectively through fluorescent integration.\cite{12,59,61,62} We prepared AIEgens nanobeads with high fluorescence intensity and superior photostability for use as novel fluorescent reporters in an SAT platform, showcasing their enhanced detection sensitivity compared with the commercial organic dye, PE.\cite{12} MEF based on metal nanostructures is another promising method for signal amplification in SAT platform. Chan et al. prepared metal nanoshells coated on the surface of QDs barcodes by using the seed-mediated method, and the products exhibited a two-order improvement in detection sensitivity when compared to QDs barcodes without metal coating.\cite{63} Liu et al. reported a robust method based on the fabrication of plasmonic magnetic microbeads, which enhances fluorescence by about 60-fold and improves the limit of detection by two orders of magnitude.\cite{64} Although some progress has been made with respect to signal amplification strategies based on the MEF effect for use in SAT, a series of obstacles has been noted to the preparation of plasmonic shell microspheres, which includes low metal surface coverage, inferior uniformity, uncontrollable localized surface plasmon resonance peaks, poor repeatability, and the need for time-consuming and tedious processes.

3.2.3  |  Reduction of background interference

Besides enhancing detection signal, a complementary approach for improving signal-to-noise ratio and increasing detection sensitivity is to decrease background signal. As we all know, non-specific binding is one major issue facing SAT in multiplexed assays, decreasing detection sensitivity, and reducing multiplexed capability. Hydrophobic interactions and electrostatic forces are two main reasons for non-specific binding.\cite{65} Many techniques have been proposed to suppress non-specific binding effects, such as the functional modification of the microsphere surface via modulation of electronegativity or by using blocking agents. Bovine serum albumin has been widely used as a blocking agent in SAT platforms.\cite{1} Polyethylene glycol and polyglycerol, kinds of polymers with special hydrophilicity and electronegativity as well as large steric hindrance, have been recognized as important materials for the inhibition of nonspecific binding.\cite{66,67} Moreover, various polymer brushes have been planted on the surface of microspheres and have been shown to be effective ways to improve detection sensitivity.\cite{68,69}

4  |  SUMMARY AND OUTLOOK

In this review, we have provided an overview of functional nanomaterial-based SAT for multiplexed biodetection and proposed possible solutions to current challenges. In summary, the performance of functional nanomaterial-based SAT has been significantly improved through the regulation of encoded microspheres and the optimization of signal-to-noise in order to address the problems of barcoding capacity and detection sensitivity, while there remains
huge potential for the further improvement of SAT to support the development of modern biomedicine and improve human health. Several challenges exist that must be urgently addressed to further improve the performance of SAT and broaden its application potential. First of all, one trend is the development of multiplexed point-of-care (POC) diagnostic platforms that combine microfluidic techniques, smartphones, and SAT, as POC diagnosis becomes more and more prevalent. Second, equipment bulk can be reduced by designing wash-free detection platforms based on SAT or by optimizing equipment structures to fulfill the demand of POC diagnosis. Third, fluorescence compensation resulting from spectral overlap or fluorescence spillover promises to present an intractable obstacle for the near future but may be overcome by the use of new decoding devices, such as spectral flow cytometry and mass cytometry, among others. Moreover, the elimination of cross-reactivity (also known as the nonspecific binding effect) is another major concern facing multiplexed detection, particularly with respect to large-scale sandwich multiplexed immunoassays, and limits the multiplexed capability of SAT. Finally, with the rapid development of artificial intelligence technology, the utilization of model simulation, machine learning, and other routes can effectively design and screen functional nanomaterials for barcoding to build SAT platforms with superior performance.

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CONFLICT OF INTEREST
The authors declare no conflict of interest.

ORCID
Wanwan Li https://orcid.org/0000-0003-3809-0737

REFERENCES
1. Y. Leng, K. Sun, X. Chen, W. Li, Chem. Soc. Rev. 2015, 44, 5552.
2. R. Wilson, A. R. Cossins, D. G. Spiller, Angew. Chem. Int. Ed. Engl. 2006, 45, 6104.
3. Y. Lu, J. Lu, J. Zhao, J. Cusido, F. M. Raymo, J. Yuan, S. Yang, R. C. Leif, Y. Huo, J. A. Piper, J. Paul Robinson, E. M. Goldys, D. Jin, Nat. Commun. 2014, 5, 3741.
4. C. Ji, P. Jiang, X. Ye, M. Chang, F. Liu, Y. Shen, D. Chen, L. Nie, Sci. Adv. Mater. 2019, 11, 680.
5. J. P. Nolan, L. A. Sklar, Trends Biotechnol. 2002, 20, 9.
6. F. Hu, C. Zeng, R. Long, Y. Miao, L. Wei, Q. Xu, W. Min, Nat. Methods 2018, 15, 194.
7. M. Dagher, M. Kleinman, A. Ng, D. Juncker, Nat. Nanotechnol. 2018, 13, 925.
8. S. Fournier-Bidoz, T. L. Jennings, J. M. Klostranec, W. Fung, A. Rhee, D. Li, W. C. Chan, Angew. Chem. Int. Ed. Engl. 2008, 47, 5577.
9. Y. Leng, W. Wu, L. Li, K. Lin, K. Sun, X. Chen, W. Li, Adv. Funct. Mater. 2016, 26, 7581.
10. D. S. Z. Zhang, Y. Jiang, H. Yang, Y. Zhu, S. Zhang, Y. Zhu, D. Wei, Y. Lin, P. Wang, Q. Fu, Adv. Funct. Mater. 2016, 26, 6146.
11. W. Wu, X. Yu, M. Gao, S. Gull, L. Shen, W. Wang, L. Li, Y. Yin, W. Li, Adv. Funct. Mater. 2020, 30, 1906707.
12. X. Wu, X. Wang, M. Shen, L. Li, Y. Yin, L. Shen, W. Wang, D. Cui, J. Ni, X. Chen, W. Li, Theranostics 2019, 9, 7210.
13. Q. Guo, Y. Wang, C. Chen, D. Wei, J. Fu, H. Xu, H. Gu, Small 2020, 16, 1907521.
14. G. Wang, Y. K. Leng, H. J. Dou, L. Wang, W. W. Li, X. B. Wang, K. Sun, L. S. Shen, X. L. Yuan, J. Y. Li, K. Sun, J. S. Han, H. S. Xiao, Y. Li, ACS Nano 2013, 7, 471.
15. X. Wang, G. Wang, W. Li, B. Zhao, B. Xing, Y. Leng, H. Dou, K. Sun, L. Shen, X. Yuan, J. Li, K. Sun, J. Han, H. Xiao, Y. Li, P. Huang, X. Chen, Small 2013, 9, 3327.
16. S. Lu, D. S. Zhang, D. Wei, Y. Lin, S. Zhang, H. He, X. Wei, H. Gu, H. Xu, Chem. Mater. 2017, 29, 10398.
17. Y. Lu, J. Zhao, R. Zhang, Y. Liu, D. Liu, E. M. Goldys, X. Yang, P. Xi, A. Sunna, J. Lu, Y. Shi, R. C. Leif, Y. Huo, J. Shen, J. A. Piper, J. P. Robinson, D. Jin, Nat. Photonics 2013, 8, 32.
18. C. Chen, P. F. Zhang, G. H. Gao, D. Y. Gao, Y. Yang, H. Liu, Y. H. Wang, P. Gong, L. T. Cai, Adv. Mater. 2014, 26, 6313.
19. L. Zhou, Y. Fan, R. Wang, X. Li, L. Fan, F. Zhang, Angew. Chem. Int. Ed. Engl. 2018, 57, 12824.
20. R. J. Fulton, R. L. McDade, P. L. Smith, L. J. Kienker, J. R. Kettman, Clin. Chem. 1997, 43, 1749.
21. J. Zhang, S. Shikha, Q. Mei, J. Liu, Y. Zhang, Mikrochim. Acta 2019, 186, 361.
22. M. Han, X. Gao, J. Z. Su, S. Nie, Nat. Biotechnol. 2001, 19, 631.
23. F. B. B. H. Wang, L. Sun, Y. Liu, Y. Zhao, J. Mater. Chem. B 2018, 6, 7257.
24. W. Wu, Y. Leng, M. Shen, W. Li, Prog. Chem. 2019, 31, 253.
25. J. Luo, Z. Xie, J. W. Y. Lam, L. Cheng, B. Z. Tang, H. Chen, C. Qiu, H. S. Kwok, X. Zhan, Y. Liu, D. Zhu, Chem. Commun. 2001, 18, 1740.
26. Y. N. Hong, J. W. Y. Lam, B. Z. Tang, Chem. Soc. Rev. 2011, 40, 5361.
27. J. Mei, N. L. C. Leung, R. T. K. Kwok, J. W. Y. Lam, B. Z. Tang, Chem. Rev. 2015, 115, 11718.
28. Y. Tang, B. Z. Tang, Principles and Applications of Aggregation-Induced Emission, 1st ed., Springer, Switzerland 2019.
29. G. Feng, G. Q. Zhang, D. Ding, Chem. Soc. Rev. 2020, 49, 8179.
30. C. Chen, X. Ni, S. Jia, Y. Liang, X. Wu, D. Kong, D. Ding, Adv. Mater. 2019, 31, e1904914.
31. X. Ni, X. Zhang, X. Duan, H. L. Zheng, X. S. Xue, D. Ding, Nano Lett. 2019, 19, 318.
32. F. Zhang, X. Liu, Z. Cheng, H. Zhang, Y. Fan, Angew. Chem. Int. Ed. Engl. 2020, 60, 1.
33. L. A. Lane, X. Qian, S. Nie, Chem. Rev. 2015, 115, 10489.
34. M. Vendrell, K. K. Maiti, K. Dhaliwal, Y. T. Chang, Trends Biotechnol. 2013, 31, 249.
AUTHOR BIOGRAPHIES

Weijie Wu received her PhD in materials science from Shanghai Jiao Tong University in 2020. She is currently a postdoctoral fellow in the School of Materials Science and Engineering & State Key Lab of Metal Matrix Composites of Shanghai Jiao Tong University. Her research interests focus on designing functional nanomaterials-based biosensors for multiplexed biodetection.

Wanwan Li obtained his PhD in materials science from Shanghai University in 2004, then he joined the School of Materials Science and Engineering & State Key Lab of Metal Matrix Composites of Shanghai Jiao Tong University in 2005, where he was promoted to a Professor in 2013. During 2012 to 2013, he joined the Laboratory of Molecular Imaging and Nanomedicine (LOMIN) at the National Institute of Biomedical Imaging and Bioengineering (NIBIB) as a visiting scholar. His research concerns fabrication of micro/nanomaterials and their applications on bioimaging and theranostics.

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