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Amphiphilic-Polymer-Guided Plasmonic Assemblies and Their Biomedical Applications

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Abstract

Plasmonic nanostructures with unique physical and biological properties have attracted increased attention for potential biomedical applications. Polymers grafted on metal nanoparticle surface can be used as assembly regulating molecules to guide nanoparticles organize into ordered or hierarchical structures in solution, within condensed phases, or at interfaces. In this Topical Review, we will highlight recent efforts on self-assembly of gold nanoparticles coated with polymer brushes. How and what kind of polymer graft can be used to adjust nanoparticle interactions, to dictate interparticle orientation, and to determine assembled nanostructures will be discussed. Furthermore, the Topical Review will shed light on the physicochemical properties, including self-assembly behavior and kinetics, tunable localized surface plasmon resonance effect, enhanced surface enhanced Raman scattering, and other optical and thermal properties. The potential of self-assembled nanostructures for applications in different fields, especially in biomedicine, will also be elaborated.

Graphical Abstract

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ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.bioconjugchem.6b00521. NMR and GPC spectra and GPS traces. (PDF)

Author Contributions

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1. INTRODUCTION

Various plasmonic nanocrystal-based assemblies (especially 3D plasmonic assemblies), exhibiting tunable localized surface plasmon resonance (LSPR) effect,¹ have recently been developed for their potential biomedical applications.^{2–4} These materials not only can be designed to function as attractive probes for cancer cell detection (by spectroscopy or imaging) but also can be used as highly localized heat sources for photothermal therapy (PTT) as well as for combined chemophotothermal therapy upon laser irradiation.^{5,6} While functioning as carriers for anticancer drugs, the heat generated by plasmonic assemblies can trigger drug release. Due to the huge potential of plasmonic assemblies for biomedical applications,^{7,8} different functional plasmonic assemblies-based probes, imaging agents, and nanocarriers, such as mesoporous silica coated,^{9,10} thermosensitive hydrogel modified¹¹ and polymer nanoparticle loaded gold nanoparticles (AuNPs),^{12,13} gold nanorods (AuNRs), AuNP clusters based on DNA linker,^{14,15} have been developed. Plasmonic assemblies are powerful platforms for ultrasensitive biosensing and bioimaging because of the tunable strong plasmonic coupling between adjacent nanoparticles. Ultrastrong interparticle plasmonic coupling in the plasmonic assemblies can induce a red shift in LSPR spectra, enhance surface-enhanced Raman scattering (SERS), and increase PTT effects and photoacoustic (PA) signals.^{16–20} Self-assembly provides a facile approach to organizing discrete nanoparticles into functional assemblies and has the potential to accommodate massively parallel, large-scale material processing for biomedical applications.²¹ A variety of self-assembly strategies, including self-assembly at fluid interfaces, convective or capillary assembly, and chemical conjugation between nanoparticles, for metal nanocrystals have been proposed to prepare plasmonic assembled nanostructures.

Assembled nanostructures of amphiphilic polymers, such as micelles, liposomes, and vesicles, have been intensively investigated.^{22,23} The balance of attractive forces, between hydrophilic and hydrophobic interactions, guides the assembly behavior of the amphiphilic

polymers.^{24,25} For example, through tuning structural parameters (such as ratio and molecular weight) of hydrophilic and hydrophobic parts of amphiphilic polymers, assembled structures can be well-controlled.²⁴ Thus, amphiphilic gold nanocrystals coated with mixed or diblock hydrophilic and hydrophobic polymers or single amphiphilic block copolymer and gold nanoparticles coated with mixed polymer as building blocks have been prepared to obtain a series of plasmonic assembly-based nanostructures (Figure 1), exhibiting enhanced scattering cross-section and photothermal conversion efficiency.^{26–28} Such plasmonic assemblies, built from polymer-coated AuNPs, inherit self-assembly properties of amphiphilic polymers and, thus, generate a series of functional nanostructures.²⁹ Graft polymers can be further used to form desired self-assembled structures and to adjust the interparticle distance and assembled orientations.

Polymer-guided assembly approach is particularly attractive for the fabrication of metal nanoparticles into desired plasmonic assemblies. This Topical Review focuses on the recent approaches to prepare plasmonic nanocomposites assembled from polymer coated gold nanocrystals, with emphasis on their unique plasmonic properties, leading to tunable LSPR, enhanced PTT property, SERS, and PA signal. We will also present their diverse biomedical applications (including biosensing, bioimaging, and nanomedicine) and finally, will discuss briefly the challenges as well as the potentials of functional plasmonic assemblies in medicine.³⁰

2. PLASMONIC ASSEMBLIES BASED ON POLYMERS

Amphiphilic diblock copolymers exhibit excellent self-assembly behavior in solution.^{25,38} These copolymers can self-assemble into a series of nanostructures such as nanoparticles, spherical and cylindrical micelles, films, vesicles, and tubes.²³ The self-assembly character of block copolymers can be induced into inorganic nanoparticle self-assemblies.^{25,39} Our group has demonstrated that amphiphilic gold nanocrystals coated with mixed hydrophilic and hydrophobic polymer brushes, as building blocks, can be self-assembled into a series of assembled nanostructures, such as dimer, film, and vesicular structures (Figure 2A).^{7,12,17,31,40–44} In the vesicular nanostructure, hydrophobic polymer forms a vesicular shell embedded with gold nanocrystals, while the hydrophilic brush extends to both the interior and the exterior sides of this vesicle. Because the vesicular shell is composed of hydrophobic polymers, the relative ratio of hydrophilic and hydrophobic polymers and molecular weight will affect the interparticle distance.⁴⁵

To facilitate the adjustment of the ratio and molecular weight of hydrophobic polymer brushes, Duan and Song et al. developed a “two-step” method, combining “grafting to” and “grafting from” approaches, to attach polymers on the surface of gold nanoparticles (Figure 2A).³¹ In the first “grafting-to” step, polyethylene glycol (PEG) and atom-transfer radical polymerization (ATRP)⁴⁶ initiator were coattached on the surface of gold nanocrystals through a covalent “Au–S” bond. In the second “grafting from” step, hydrophobic brushes were grown on the surface of gold nanocrystals using ATRP approach. This in situ method of growing the surface polymer brush shows several advantages: (1) it allows adjustment of the ratio of hydrophilic to hydrophobic brushes; (2) it facilitates grafting of different functional polymers on the surface of nanoparticles; and (3) it controls polymer molecular

weight easily by adjusting reaction time and temperature. Gold nanoparticles coated with diblock amphiphilic polymer can also be self-assembled into cylindrical micelles, chains, and vesicles.⁴⁷

Gold nanoparticles coated with a single amphiphilic diblock polymer exhibit similar assembly behavior as block copolymer and can be self-assembled into a variety of nanostructures. Liu et al. reported ultrasmall (<4 nm) gold nanoparticles attached with a single amphiphilic triblock copolymer chain per NP, capable of spontaneous self-assembling into a series of nanostructures including micelles, vesicles, and rods in aqueous solution (Figure 2B).³⁵ The small AuNP hybrid amphiphilic triblock copolymers, poly(ethylene glycol)–AuNP–poly(styrene) (PEG–AuNP–PS), act as the polymer–metal–polymer analogue of conventional amphiphilic triblock copolymers. In this assembled nanostructure, the AuNPs are located at the interface of the assemblies because the hydrophobic AuNPs are sandwiched between PEG and PS outer domains. However, there is nearly no physical difference between the vesicle and single nanoparticles because of the negligible plasmonic coupling between the neighboring small AuNPs, thus limiting their biomedical applications.

Another well-known approach to self-assemble plasmonic metal nanoparticles is to use polymer as template. Zhu group demonstrated that PS-coated AuNPs (Au@PS) with different sizes can be precisely localized at the center or the interface of hybrid PS-*b*-P4VP cylindrical micellar aggregates (Figure 2C).³⁶ The probable mechanism could be the rearrangement of PS and P4VP ligands on the AuNP surface during the assembly process, which induces strong adsorption of AuNP@PS to the interface of polystyrene-*b*-poly(4-vinylpyridine) (PS-*b*-P4VP) domains. Watkins group have systematically studied the spatial distribution of gold nanoparticles of different sizes in symmetric polystyrene-*b*-poly(2-vinylpyridine) (PS-*b*-P2VP) through hydrogen bonding-mediated assembly (Figure 2D).³⁷ The H-bonding interactions between polymer and AuNP lead to adjustable enthalpic interaction to prevent inherent entropy penalties that arise from block copolymer chain stretching upon the sequestration of large AuNPs. This method introduces a strategy to place large AuNPs within polymer templates for the preparation of well-ordered hybrid composites.

3. TUNING LSPR

When plasmonic nanocrystals form assemblies or aggregates, the surface plasmon absorption of newly formed structures depends on the interparticle distances and can red-shift LSPR to the NIR region.^{42,50–52} For the plasmonic assemblies based on polymer strategy, polymer grafts on AuNP surface serve as molecular spacers, adjusting gold nanoparticle separation distances during the self-assembly process. In the case of plasmonic gold nanovesicles, the LSPR of vesicle can be easily adjusted between visible and the NIR region through tuning the interparticle distance inside vesicular shell. For example, Duan et al. have prepared photoresponsive vesicles assembled from 14 nm gold nanoparticles coated with PEG and PNBA (Au@PEG/PNBA) and found that the LSPR shift is highly dependent on the relative ratio of PEG to hydrophobic PNBA chains (Figures S1 and S2), with decreasing PEG fraction resulting in a marked red shift.⁴⁵ With the decreased ratio of PEG, the hydrophobic property of the gold nanoparticle increased, while the interparticle distance

of vesicle membrane decreased, inducing a larger LSPR red shift. With the decreasing ratio of PEG to PNBA from 1:1 to 1:4, a spectral shift from 550 nm to 745 nm was observed, suggesting a decrease in the interparticle distance and enhanced plasmonic coupling (Figure 2A).⁴⁵ Duan et al. also reported that the LSPR peak of AuNR@PEG/PLA vesicle exhibited more red-shift with decreasing ratio of PEG to PLA (Figures 3B, S3, and S4). The reason could be attributed to decreased hydrophilicity of the amphiphilic gold nanoparticles that lead to closer attachment of gold nanoparticles. These findings confirm that plasmonic coupling in plasmonic assemblies is dependent on the ratio of hydrophilic and hydrophobic brushes on the surface of gold nanoparticles.

Apart from interparticle distance, shape and size of assemblies also play vital roles in the plasmonic coupling effect, thus affecting the LSPR.⁴⁹ In another study, Chen et al. found that the size of vesicles increased with increase in nanoparticle concentration, leading to stronger plasmonic coupling and red-shifting of LSPR.⁴⁰ Zhang et al. observed changes in absorption peak and a larger red shift in LSPR with an increased size of plasmonic gold nanomicelles, as displayed in Figure 3C.⁴⁸ Moreover, physical properties of polymer brush affect assembled structures and interparticle space. Compared with the Au@PEG-*b*-PS vesicles, the Au@PEG-*b*-PCL vesicles exhibited more LSPR red-shifting, with the major peak at 1008 nm, determined based on the molecular weight of PS and PCL being the same.⁴⁰ The reason could be attributed to more flexibility of PCL over PS, inducing stronger plasmonic coupling. This strategy may facilitate fine control of the interparticle distance, thus adjusting the physical properties of Au@PEG-*b*-PCL vesicles.

Furthermore, the effect of morphology and orientation of assembled nanocrystals on LSPR have been investigated. Tao et al. recently reported that LSPR peak of plasmonic assembly shifts according to the orientation of metal nanocubes.⁵³ These polymer brush modified metal nanocubes self-assembled into arrays of one-dimensional strings with face-to-face, face-to-edge, and edge-to-edge orientations possess tunable interparticle distances and adjustable electromagnetic properties, depending on the extent of plasmonic coupling. Importantly, the properties of such assemblies strongly rely on various parameters, such as polymer chain length, grafting density, and rigidity of the polymer grafts used in the study.

Interestingly, the disassembly process of assembled AuNP nanostructures can also cause spectral changes; therefore, reversible assembled and disassembled nanostructures of AuNPs with tunable LSPR can be attractive nanomaterials. Li et al. prepared a stress-responsive colorimetric plasmonic film using polymer coated-AuNP.⁴⁹ Accurate determination of the stress experienced by the film is possible because the film memorizes the plasmonic shift during disassembly process of 1D AuNP chains driven by plastic deformation of the covering polymer matrix (Figure 3D). In another study, Yin et al. prepared a thermoresponsive plasmonic AuNP chain by self-assembling the PNIPAM-coated AuNPs in aqueous solution, which exhibited reversible LSPR by controlling solution temperature.¹¹ This thermoresponsive AuNP chain with reversible dynamic tunable LSPR is a promising material to be applied for LSPR-based functional optical devices.

Amphiphilic-polymer-directed assembly is a facile method by which to organize plasmonic metal nanoparticles into diverse nanostructures with tunable and responsive optical

properties. Via this method, metal nanoparticles coated with amphiphilic-polymer brushes with a specific ratio of hydrophilic and hydrophobic polymers can be assembled into a series of nanostructures, including dimer, clusters, micelles, chains, film, vesicles, and other complex nanostructures. The assembly process is governed by intermolecular forces (such as hydrophobic-hydrophobic interaction) rather than chemical bonds between metal nanoparticles. Thus, the assembly nanostructure is also dependent on the parameters of polymers, such as molecular weight, polymer length, graft density, and miscibility.

4. SURFACE-ENHANCED RAMAN SCATTERING

Recent advances in plasmonics, especially stimuli-responsive well-defined plasmonic assemblies, have attracted considerable research efforts in SERS-based sensing materials, which are promising for the spectroscopic detection of molecular, cellular, and in vivo targets.^{54–56} Mild aggregation of plasmonic nanoparticles induces intense electromagnetic field enhancement in the space (“hot spot”) between adjacent AuNPs. When the Raman reporter is placed in the “hot spot”, the Raman signal is enhanced significantly.^{57,58} In comparison with single nanocrystals, plasmonic assemblies are more attractive because they offer many hot spots with greatly enhanced functionality and sensitivity.⁵⁹ Recent work in our group demonstrated that interparticle plasmonic coupling in the plasmonic vesicular shell can significantly amplify the SERS signal of Raman reporters, thus making the detection of the surface coating-mediated assembly and disassembly of SERS-encoded nanoparticles possible using Raman spectroscopy.³¹ The Raman signal from the AuNR@PEG/PLA vesicles coated with the Raman reporter 2-naphthalenethiol is 24 times stronger than that of single AuNR, exhibiting an enhancement factor of 5.7×10^6 . We have successfully exploited pH- and enzyme-responsive plasmonic vesicles, prepared by self-assembly of gold nanoparticles attached with Raman reporter, for the sensitive tracing of cargo release and cancer cell detection. The acidic environment of cancer cell and enzyme induce the decrease or disappearance of the SERS signal.

To fulfill different biomedical requirements, SERS enhanced assemblies can be well-designed and prepared accordingly by using the polymer guided strategy.^{38,41} For instance, Walker et al. have proposed a facile approach to preparing functional AuNR dimers or chains that provide a strong SERS signal useful for bright plasmonic, temporally stable biosensors in the solution state (Figure 4A).¹⁸ The method involves end-functionalization of AuNRs with PS that enables end-to-end self-assembly of AuNR dimers and chains and controls the gap size through PS molecular weight (MW). The results showed that AuNR chains exhibit ~550 times greater SERS intensity than did a single AuNR (and ~750 greater than Raman dye) depending on the inter-rod gap size, as shown in Figure 4B – D. Tao and co-workers prepared arrays of one-dimensional strings by self-assembly of polymer-grafted metal nanocubes, having well-defined interparticle orientations (face-to-face, face-to-edge, and edge-to-edge) and tunable electromagnetic properties depending on the assembled orientation and intercube distance, as displayed in Figure 4E,F.⁵³

5. ENHANCED PHOTOTHERMAL PROPERTY

Gold-based plasmonic nanocrystals or assemblies represent a new generation of inorganic nanomaterials for cancer theranostic applications. Polymer coating on AuNP surfaces not only offers the drive to tune the LSPR of AuNPs assemblies but also can transfer AuNPs into photothermal conversion reagents under NIR laser irradiation. Because the absorption peak of plasmonic vesicles can be tuned to NIR region, the photothermal property of vesicles has been investigated.^{40,48} We found that upon irradiation with NIR laser at 1 W/cm² for 5 min, the temperatures of AuNPs (at the same gold concentration as that of the Au@PEG-*b*-PCL vesicles, $\lambda_{\text{ex}} = 808$ nm), AuNRs (OD@808 nm = 1, $\lambda_{\text{ex}} = 808$ nm), Au@PEG-*b*-PS vesicles (OD@671 nm = 1, $\lambda_{\text{ex}} = 671$ nm), and Au@PEG-*b*-PCL vesicles (OD@808 nm = 1, $\lambda_{\text{ex}} = 808$ nm) were raised by 8, 24, 23.6, and 40.7 °C, respectively.⁴⁰

The photothermal conversion efficiency of Au@PEG-*b*-PCL vesicle is 37%, which is higher than that of gold nanoshells (13%), AuNR (22%), and Au@PEG-*b*-PS vesicle (18%).⁴⁰ The enhanced photothermal conversion efficiency of Au@PEG-*b*-PCL vesicles can be attributed to the strong interparticle plasmonic coupling that increases the extinction efficiency of the vesicles. Importantly, the temperature increase of the Au@PEG-*b*-PCL vesicle is directly proportional to vesicle concentration, NIR laser energy or laser irradiation time. Moreover, in a recent study, we found that ultrasmall AuNR@PEG/PLGA vesicles of amphiphilic AuNR@PEG/PLGA exhibit enhanced the photothermal effect in comparison with individual AuNRs (Figure 5A–C) and demonstrate excellent therapy effect for NIR-laser triggered cancer cell killing and tumor therapy.³⁴

In a recent work, through a polymer template method, Zhang group⁴⁸ reported a new kind of gold nanomicelles assembled from comblike amphiphilic-polymer-coated AuNPs (6 nm) with excellent photothermal property (Figure 5D), which can be utilized as NIR PTT agent. Because these gold nanomicelles were assembled from AuNPs of 6 nm size, they could be disintegrated into single AuNPs and subsequently cleared from the body post-therapy.

6. PHOTOACOUSTIC PERFORMANCE

Plasmonic nanomaterials, such as AuNP, AuNR, gold nano-shells, and gold nanostars with efficient NIR region absorption properties and strong PA performance, are potential candidates for biomedical applications.^{61–63} The optical absorption mechanism of these gold nanostructures is based on LSPR.⁶⁴ These nanomaterials exhibit enhanced PA signal due to the enhanced photothermal effect generated by strong plasmonic coupling of the plasmonic assemblies.⁶⁵ As is evident from Figure 6, the AuNR@PEG/PLGA vesicles exhibit increased PA signals compared to those of individual AuNRs at the same value of optical density at 808 nm (OD₈₀₈). The PA intensity of the vesicles is linearly correlated with vesicle concentration ($R^2 = 0.994$) (Figure 6B).³⁴

The strong PA signal of the vesicles makes it possible to investigate its further application for biomedical imaging.⁴⁰ As shown in Figure 6C, a strong PA signal is observed in the tumor region after intravenous injection of the vesicles. These vesicles, containing polymer-

coated AuNP, are fully covered by high-density polymers, such as PEG, guaranteeing their biological stability and safety for theranostic applications.³¹

To further increase PA performance of the plasmonic vesicles, Nie et al. developed a new type of plasmonic AuNP vesicles with vesicular shells containing strings of AuNPs grafted with amphiphilic block copolymer PEG-b-PS.³⁹ The density and molecular weight of the block copolymer determine the formation of chain plasmonic vesicles. These vesicles exhibit a stronger absorption than the vesicles containing AuNPs in the NIR region, indicating its higher efficiency and performance in photoacoustic imaging.

We recently prepared a hybrid gold nanoparticle coated carbon nanotube ring (CNTR@AuNP) using redox-active polymer brush as the template and reducing agent.⁶⁶ Both the density and size of the coated gold nanoparticles can be controlled easily by adjusting the graft density and molecular weight of the polymer brush. The adjustable LSPR of the assembly allows the designing and fabricating of stimuli-responsive nanostructures for biological applications, which cannot be achieved by single nanoparticles, such as gold nanorods and nanoshells.⁶⁷ The PA signal in the tumor region decreases with the disassociation of the gold nanoparticle vesicles upon laser irradiation.

7. CONCLUSIONS

This Topical Review discussed the recent developments in the field of self-assembly of amphiphilic-polymer-coated gold nanoparticles with excellent thermal and optical properties. Such polymer–nanoparticle composites will certainly pave the way for exploring new smart nanomaterials with tunable properties and negligible toxicity. With the development in the field of polymer chemistry and nanoparticle surface modification approaches, more functional and responsive assemblies can be designed for self-assembly of gold nanoparticles. These self-assembled gold nanoparticles will potentiate future applications in the fields of bioengineering, bioimaging, and biomedicine.

The specific future works are proposed in the following aspects: (1) functional and responsive polymers should be introduced onto nanoparticle surface to prepare stimuli-responsive assemblies, which is crucial for their biomedical applications; (2) recent developments in inorganic nanocrystal synthesis and functional biopolymer preparation have opened a wealth of possibilities by which to expand this amphiphilic polymer brush directed assembly concept to other types of nanocrystals (such as iron oxide and quantum dots) and to integrate different types of nanocrystals into multifunctional assemblies; (3) the delivery of anticancer drugs and other therapeutic agents for combined therapy, such as the hydrophobic shell and cavity the vesicle, can be used to load both hydrophilic and hydrophobic molecules; and (4) the assemblies containing biodegradable polymers can be extended to in vivo and even clinical applications. Thus, the diameter should be reduced to be in the range of 30–100 nm. The toxicity, biocompatibility, pharmacokinetics, and biodistribution of those assemblies should be systemically assessed in vivo before potential clinical translation.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Figure 1.

Schematic illustration of polymer-coated gold nanoparticles and their assemblies. Gold nanoparticles coated with functional polymer brushes, amphiphilic diblock copolymer brushes, or mixed hydrophilic and hydrophobic polymer brushes can be self-assembled into a variety of nanostructures, such as dimer, trimer, chain, cluster, micelle, vesicle, and so on.

Figure 2.

Self-assembled gold nanostructures induced by polymers. (A) Self-assembly of gold nanoparticles coated with mixed hydrophilic and hydrophobic polymer brushes into dimers (A1), film (A2), gold nanoparticle vesicles (A3) and gold nanorod vesicles (A4). (B) Schematic description of self-assembly of ultrasmall gold nanoparticles (2.0-3.8 nm) coated with a single triblock copolymer chain, into vesicle, micelle, and rod nanostructures. (C) Schematic illustration of the intermolecular hydrogen bonding directed supramolecular assembly method to prepare hybrid micellar composites with adjustable localization of the

gold nanoparticles (C1). TEM images of cross-sections of polystyrene-*b*-(4-vinylpyridine) (PS-*b*-P4VP) films incorporated with gold nanoparticle grafted with poly(styrene) (Au@PS) (C2) and hybrid cylindrical micellar composites with AuNPs localized at the center (C3). (D) Schematic illustration of the self-assembly of polystyrene-*b*-(2-vinylpyridine) (PS-*b*-P2VP) and hydroxylated AuNPs through H-bonding between P₂VP block of the BCP and ligands on the surface of AuNP (D1), TEM images of three kinds of AuNPs with different sizes localized in the center of the polymer component (D2). Reprinted with permission from refs 33 (A1), 32 (A2), 34 (A3), 31 (A4), 35 (B), 36 (C), and 37 (D). Copyright 2011, 2012, 2013, 2014, 2015, 2016, American Chemical Society and 2015, John Wiley.^{31–37}

Figure 3.

(A) UV-vis spectra of AuNPs (red line), Au@PEG/PNBA vesicles assembled from amphiphilic Au@PEG/PNBA with the ratio of PEG to PNBA of 1:1 (green line), 1:2.5 (black line), 1:3 (blue line), 1:4 (purple line), and 1:5 (yellow line). (B) UV-vis spectra of AuNR@PEG/PLA in chloroform (blue line), and AuNR@PEG/PLA vesicles assembled from AuNR@PEG/PLA with the PEG-to-PLA ratio of 1:2.5 (green line), 1:3.5 (red line), and 1:4.5 (blue line). (C) TEM images and UV-vis spectra of 6 nm AuNPs, small clusters, and micelles assembled from comb polymer coated 6 nm AuNPs. (D) UV-vis spectra of

AuNPs and polymer composite film after giving different pressures for 1 min. (E) The continuous wavelet transformation of the spectra in (A). Reprinted with permission from refs 48 and 49, copyright 2014, American Chemical Society and copyright 2015, John Wiley.

Figure 4.

(A) Preparation of lipid-encapsulated AuNR chains: (a) CTAB-coated AuNRs. (b) Polystyrene was conjugated at the ends of AuNRs through covalent Au-S bond. (c) Raman reporter (oxazine 725) was introduced to the AuNR solution in DMF, followed by the self-assembly initiated via injection of water. (d) Phospholipid solution was added to encapsulate AuNR chains. (B) SERS spectra of AuNR solutions utilizing a 5 kDa PS linker before (bottom) and after (top) AuNR self-assembly encapsulation and dialysis. (C) Comparison of experimental (black, solid) and calculated (red, dashed) enhancement. (D) Theoretical

electromagnetic field intensity models (in V/m^2) of AuNR monomers and dimers, indicating the enhancement effect upon plasmonic coupling. (E) Self-assembly of metal nanocubes into edge-to-edge and face-to-face orientations by attaching their surfaces with different molecular weight polymer brushes. (F) Electric field strength for metal nanocubes with three assembled orientations: face-to-face, face-to-edge, and edge-to-edge. Reprinted with permission from refs 18 and 53. Copyright 2014, American Chemical Society and 2015, Nature Publishing Group.

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Figure 5.

(A) Plasmonic gold nanorod vesicle assembled from AuNR@PEG/PLGA. Photothermal images (B) and temperature variations (C) of the samples in water irradiated with 808 nm laser. (D) Schematic illustration of the gold micelles assembled from polymer brush coated gold nanoparticle and their photothermal therapy in vivo. Reprinted with permission from refs 17, 34, and 60. Copyright 2013, American Chemical Society and 2015, John Wiley.

Figure 6.

Photoacoustic (PA) images (A) and PA amplitude (B) of AuNR vesicle and AuNR in water illuminated with 808/671 nm laser as a function of OD value at 808 nm. (C) Photoacoustic (PA) images (2D and 3D) of U87&MG tumor prior and 2, 6, and 24 h post-intravenous injection of ultrasmall AuNR@PEG/PLGA vesicles and individual AuNR@PEG, respectively. Reprinted with permission from ref 34. Copyright 2015, John Wiley.