Engineering of plasmon-resonant nanostructures for biomedical applications

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Abstract

Interest in metal nanostructures stems from their unique optical properties related with single-particle or collective plasmons. This report is focused on optical properties of gold nanorods and silica/gold nanoshells, whereas the synthesis protocols and biomedical applications are discussed shortly. Our consideration includes the following topics: (1) depolarized light scattering by gold nanorods; (2) sensitivity of longitudinal dipole plasmon to dielectric environment; (3) scaling properties of nanorod multipole plasmons; (4) engineering of silica/gold nanoshells for tunable optical properties; (5) collective plasmons in self-assembled nanoshell monolayers; (6) applications of plasmon-resonant particles to solid-phase immunoassay, photothermal therapy, and OCT.

1 Introduction

Gold plasmon-resonant nanoparticles have found various applications in nanobiotechnology and biomedicine [1] due to their exceptional biocompatibility. An additional advantage of such nanostructures is related to their spectral tuning of the localized plasmon resonance (LPR) by variation of metal, size, shape, structure and dielectric environment. The last property includes both the local dielectric environment formed by adsorbed probing or target molecules, and the global dielectric properties of a liquid medium, dielectric solid matrix, or dielectric substrate with dissolved, embedded, or adsorbed particles, respectively. Attachment of biomolecules to the nanoparticle surface due to physical adsorption or covalent binding via thiol-modified sites is called functionalization [2], and the functionalized nanoparticles are often called bioconjugates. Until quite recently, the colloidal gold nanosphere bioconjugates were used in the majority of biomedical applications [3]. New activities have been further motivated by recent advances in metal nanoparticle synthesis, including nonspherical and/or inhomogeneous particles such as gold nanoshells [4], nanorods [5], "nanorice" [6], "nanostars", etc. These new nanostructures allow for easy tuning of their spectral, scattering, and absorption properties. Furthermore, the collective electromagnetic response of multiparticle ensembles also shows rich optical properties and great promise to meet the rigorous demands of biodiagnostics and nanomedicine.

Here we discuss the optical properties and possible applications of two popular types of nanoparticles, viz. gold nanorods and silica/gold or polystyrene/gold nanoshells. Inhomogeneous broadening of the extinction spectra caused by the particle polydispersity and the surface-electron scattering has been studied by Westcott et al. [7]. By contrast to this study, we report on the mechanisms of spectral broadening in polydisperse ensembles as probed by the *differential light scattering* technique. For gold nanorods, our consideration is focused on the depolarized light scattering by usual small rods and on the scaling properties of multipole resonances exhibited by larger particles. The optics of interacting nanoparticles is exemplified by a self-assembled monolayer of nanoshells. It has been reported [8] that the extinction spectrum of a silver particle monolayer exhibits sharp resonance peak related to excited quadrupole and suppressed dipole resonances. Our simulations and experiments show that this feature of the monolayer collective response has a general physical basis and does not depend on the single-particle properties. In the final section of this report

we discuss shortly some up-to-date biomedical applications of functionalized plasmon-resonant nanoparticles.

2 Gold nanorods

In the Rayleigh (dipole) approximation, a small gold or silver nanorod exhibits two plasmon resonances corresponding to the excitation of a particle along and perpendicular to its major geometrical axis. In the dipole approximation, the resonance wavelengths are given by expression $\lambda_{\mathrm{P},\perp} = \lambda_p \sqrt{\varepsilon_{ib} + (1/L_{\mathrm{P},\perp} - 1)\varepsilon_m}$, where λ_p is the bulk electron plasma wavelength, ε_{ib} is the interband contribution of valence electrons to the bulk dielectric function, $L_{\mathrm{P},\perp}$ are the so-called geometrical depolarization factors, and ε_m is the dielectric function of the surrounding medium. The geometrical depolarization factors strongly depend on the particle shape, so the LPR peak position can easily be tuned by variation in the particle aspect ratio.

It is well known (van de Hulst, 1957; Kerker, 1969) that the depolarization ratio of the scattered intensities $I_{\mathrm{vh}} / I_{\mathrm{vv}}$ cannot exceed 1/3 for "usual" small randomly oriented particles. However, for plasmon-resonant particles, this constrain does not hold and the upper limit for depolarization ratio is equal to ¾ [9, 10]. Our theoretical analysis, based on the Rayleigh approximation[1] and the exact T-matrix calculations, together with experimental measurements confirmed the existence of unusual depolarization properties of gold nanorods.

To date, the dipole plasmon resonances of metal nanorods have been studied in details both theoretically and experimentally. During past 5-8 years, there appeared several observations of multipole plasmon excitations in gold and silver nanowires deposited onto a substrate (see, e.g., [11] and references therein) and gold nanorods suspended in water [12]. Here we report on the relationships between the multipole plasmons of nanorods and their size, shape, and orientation with respect to polarized incident light. We have found that the multipole resonance wavelengths as a function of the aspect ratio divided by the resonance number collapse onto one linear curve [13] (Fig. 1). This scaling property is explained by using the plasmon standing wave concept [14].

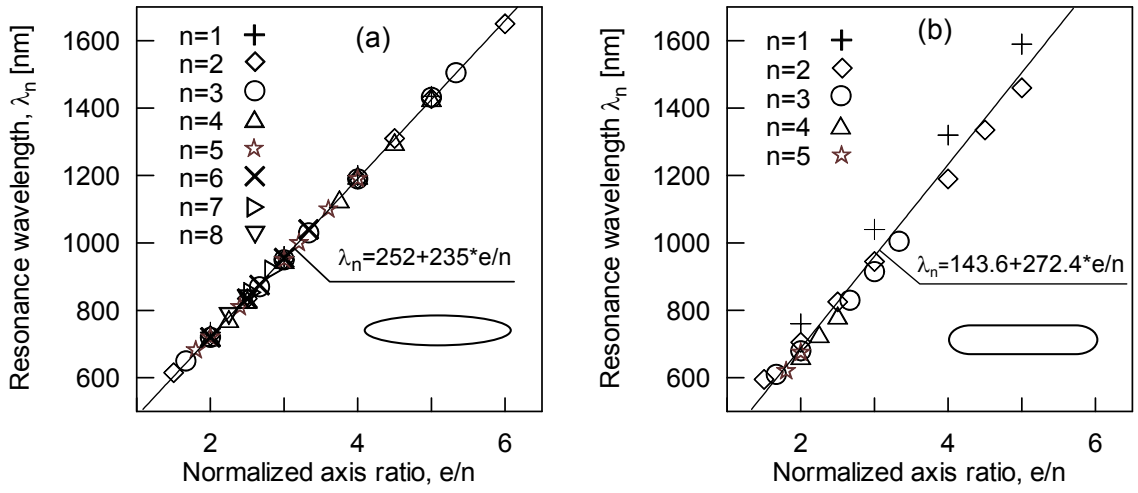

Fig. 1. The linear scaling of multipole resonance wavelengths λ_n *vs* normalized aspect ratio e/n. Calculations for randomly oriented gold spheroids (a) and s-cylinders (b) in water. The particle diameter $d = 80$ nm, the aspect ratio $e = L/d$ = 2-20 (a), 2-12 (b), and the extinction resonance number $n = 1-8$ (dipole, quadrupole, etc.).

[1] Recently, our conclusions about upper depolarized ratio limits for metal and dielectric particles were reproduced by Calander et al. (Chemical Physics Letters **434**,326–330 (2007)) by using a similar Rayleigh approximation analysis.

3 Silica/Gold nanoshells

The effects of the gold nanoshells structural polydispersity and the surface electron scattering in a thin metal layer on the resonance light scattering spectra are studied theoretically and experimentally for the silica/gold nanoshell water colloids. To test the calculations experimentally, two samples of nanoshells (designated 1 and 2) were synthesized. According to the dynamic light scattering data, the sample 1 particles have a 90-nm diameter of core and a broad shell thickness distribution (with an average value of 30 nm), whereas the sample 2 particles have a 70-nm diameter of core and a narrow shell thickness distribution (with an average value of 12 nm). For sample 1, the inhomogeneous broadening of the scattering spectrum is completely determined by the polydispersity; therefore, the bulk constants of gold can be used in simulation of the particle spectra. For sample 2, the main mechanism of the broadening is related to the limitation of the free path of electrons, whereas the contribution from the shell thickness distribution can be neglected.

Recently, Chumanov's group [8] reported on some interesting optical properties of interacting silver nanospheres assembled into 2D array and possessing the dipole and quadrupole single-particle resonances. Here we extend these observations for several kinds of nanostructures to illustrate the general physical basis of the dipole resonance suppression phenomenon. The extinction, scattering, and absorption spectra of silver and gold nanosphere and nanoshell 2D monolayers were calculated by the generalized multiparticle Mie solution. Because of the coherent interaction among particles in the array, the dipole band of extinction disappeared and only the quadruple component of the spectra was observed. In the experimental section, we examined the suspensions and 2D self-assembled arrays of nanoshells with a silica core diameter of 210 nm and a gold shell thickness of 28 nm. Although the dipole resonance suppression phenomenon was not as spectacular as in the case of silver nanospheres, we observed qualitative agreement between the experimental and theoretical data.

4 Biomedical applications

Both the gold nanorods and nanoshells are exceptionally biocompatible nanomaterials, which surface can be easily functionalized by key probe molecules such as antibodies, oligonucleotides, biotin, protein A, lectins, enzymes, etc. Such hybrid nanoparticle-molecule structures are basic build blocks for biosensorics, targeted drug or gene vectors delivery, photothermal therapy, and biomaterial imaging based the dark-field light microscopy, laser confocal microcopy, or OCT techniques. Recent reported examples are application of these techniques to cancer cell experiments in vitro [15] and OCT imaging with gold nanoshells and nanorods [16].

Last year, at St.-Petersburg ELSN-9 Conference, we demonstrated a short dark-filed microscopy movie to visualize the dynamic behavior and interaction of gold nanorods and rat macrophages. Quite recently, Cortie group reported on successful photothermal destruction of murine microphages labeled with gold-nanorod-monoclonal-antibody conjugates [17].

In this report, we discuss our recent first application of silica-gold nanoshells to a solid-phase dot immunoassay [18]. The assay principle is based on staining of a drop (1μL) analyte on a nitrocellulose membrane strip by using silica/gold nanoshells conjugated with biospecific probing molecules. Experimental example is human IgG (hIgG, target molecules) and protein A (probing molecules). For usual 15-nm colloidal gold conjugates, the minimal detectable amount of hIgG is about 4ng. By contrast, for nanoshell conjugates (silica core diameter of 70 nm and gold outer diameter of 100 nm) we have found significant increase in detection sensitivity and the minimal detectable amount of hIgG is about 0.5 ng. This finding is explained by the difference in the monolayer particle extinction.

Finally, we provide an illustration of erythrocyte and living bacteria imaging with silica-gold nanoshells as resonance-scattering labels. In this case, nanoshells are seen as bright red dots against a dark background, except for yellow areas of aggregation, where nanoshells are in close proximity and the plasmon resonance wavelength is changed.

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