

Applications of Hybrid Metal Nanoparticle-Quantum Dot in Biomedical Applications

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Abstract— Nanomaterials are at the forefront of the fast-paced development of nanotechnology. These materials are outstanding and indispensable in various human activities as long as their size-dependent characteristics. One of the most promising applications of nanomaterials is biomedical. This work reviews the hybrid quantum dot-metal nanoparticle applications in biomedical. An analytical model for the double quantum dot–metal nanoparticle system is proposed, and the system exhibits high susceptibility, which can be used in biomedical applications.

Keywords— Double quantum dot, Plasmonics, biomedical.

I. INTRODUCTION

Nanotechnology is generated on three levels: materials, devices, and systems, as it deals with nanometer-sized objects [1]. Nanomaterials are currently the most advanced scientific understanding and commercial applications. Nanoparticles have been studied for over a decade due to their size-dependent effect on physical and chemical properties [2]. They are now in the commercial exploration phase [3,4].

Nanotechnology research is fueled by a desire to better understand biological activity at the Nanoscale [5]. The average diameter of a cell in a living animal is 10 nanometers. On the other hand, The cell pieces are much smaller, measuring in the sub-micron range. Like the tiniest artificial nanoparticles, proteins are smaller, with an average size of just 5 nm. Nanoparticles could be employed as tiny probes to examine cellular machinery without creating too much disturbance because of their small size [6].

Semiconductor quantum dots (QDs) have been extensively explored in recent decades due to their remarkable optical properties: strong photoluminescence, tunable color, and great photostability. Due to their light-scattering and surface plasmonic capabilities, metal nanoparticles (MNPs) have also piqued the research interest [1, 2]. Modern nanotechnology allows for the fabrication of a variety of nano-superstructures. A hybrid structure of QDs and MNPs has recently attracted interest [7-15]. When a QD is positioned near an MNP, the QD and MNP can be electronically coupled, and the hybrid geometry determines the coupling strength. As a result of such hybridization, Fano-type asymmetric patterns in absorption spectra [1,2], exciton/plasmonic-driven transparency [5,8], and accelerated Rabi flipping [15] have all been demonstrated. Here, the biomedical applications of hybrid MNP-QDs are reviewed, and their applications are discussed. The rest of this work deals with applications in section 2, and recent developments are reviewed in section 3. The theory is presented in section 4, while the work is concluded in section 5.

II. APPLICATIONS

Nanotechnology applications in medicine are up-and-coming, and disciplines like illness detection, drug delivery targeted at specific places in the body, and molecular imaging are all being researched extensively, with several items already undergoing clinical trials. According to recent technical advancements, nanotechnology will significantly impact disease prevention, diagnosis, and treatment. Small molecules with a 1000 Da or less mass that circulate systemically make up most of today's medications. Toxicity to nontarget organs, difficulty maintaining drug



concentrations within therapeutic windows, and drug metabolism and excretion are common side effects of systemic biodistribution, limiting efficacy. Nanotechnology-based delivery methods could alleviate these problems by combining tissue- or organ-specific targeting with therapeutic action. Multifunctional nano-delivery systems could connect targeted, diagnostic, and therapeutic activities. In a precisely controlled manner, nanotechnology advancements have led to the designing and construction of structures at the nanometer scale. Nano-probes (particles smaller than 100 nm) are enhanced nanostructures that have sparked interest in biological and clinical research. Nanoscale systems, unlike macroscale structures, have optical and electronic properties that the structure's size, shape, and material composition can control. Engineers, clinicians, and researchers can use these features to create an endless supply of precursor materials for imaging contrast agents, optical switches for drug release triggering, and therapy [16].

One of the first applications of nanomaterials will be improved fluorescent markers for diagnostic and screening reasons. Semiconductor nanocrystals are more stable and have a narrower, adjustable, symmetric emission spectrum than traditional fluorophores. They can be used as fluorescent probes in biological staining and diagnostics, complement existing fluorophore probes, and are superior [17]. In ultrasensitive biological detection, QDs have been covalently attached to biomolecules. They are 20 times brighter, 100 times more photobleach resistant, and one-third the width in spectral linewidth. In cultured cells, QDs tagged with the protein transferrin underwent receptor-mediated endocytosis [18]. Over the last 50 years, noninvasive imaging techniques have significantly impacted medicine. The current focus is techniques like functional magnetic resonance imaging (MRI) that enhance spatial resolution and contrast agents. Intracellular imaging is already possible with nanotechnologies, thanks to the attachment of QDs or synthetic chromospheres to specific molecules, such as proteins, or the incorporation of naturally occurring fluorescent proteins, which can be investigated directly using optical techniques such as confocal microscopy and correlation imaging. A novel drug that is small enough to pass through capillary walls has been developed. An intravenous contrast agent, a bone marrow contrast agent, and a long half-life perfusion agent for the brain, heart, and liver might be employed with ultrasmall superparamagnetic iron oxide [19]. Imaging of the human (or any) body has improved. A disease must first be diagnosed before it can be treated. In addition, nanomaterials can be used to detect pathogens. Using a bead array counter, a multi-analytical biosensor to hybridize DNA and magnetic microbeads, and large antimagnetic sensors to detect and identify biological warfare agents. The defense can use such a device in the future [20].

Another application of nanotechnology is the delivery of antigens for vaccination. In terms of disease prevention, mucosal immunity is crucial. Recent developments in encapsulation and advances in suitable animal models have demonstrated that micro and nanoparticles can enhance immunization. In medicinal chemistry, functionalized carbon nanotubes (CNTs) hold much potential. Researchers found anti-peptide solid

antibody responses in mice after linking a neutralizing cell epitope from the foot-and-mouth disease virus to CNTs [21]. In addition, nanoparticle formulations can detect a protein by determining the presence of a target protein [22] and examining the structure of DNA [23]. Biomimetics has attracted great interest in biomedical fields using nanohybrid coatings with inorganic ceramic and organic copolymer elements to cover surfaces of bone tissue [24]. Nanotechnology is providing novel therapeutic opportunities for many agents that cannot be used effectively as conventional oral formulations due to poor bioavailability. Among them is the destruction of the tumor by heat (hyperthermia). Scientists have developed magnetite cationic liposomes (MCLs) as a new hyperthermic heating medium. MCLs were employed to heat subcutaneous solid glioma tissues in mice. After three repeated heating times, the researchers found complete tumor regression in 90% of the mice [25]. Ultimately, the research could yield a tiny pill that will travel through the body and thoroughly diagnose the patient's health.

III. RECENT DEVELOPMENTS OVERVIEW

A. Photodynamic cancer therapy

The death of cancer cells by laser-generated cytotoxic atomic oxygen is the basis of photodynamic cancer therapy. Cancer cells take in a more significant amount of a particular dye (photosensitizer) designed to destroy cancerous and precancerous cells used to produce atomic oxygen than healthy tissue. Hence, the cancer cells are activated by a specific wavelength of light energy, usually from a laser after light activation. Unfortunately, the residual dye molecules move to the patient's skin and eyes, making them extremely sensitive to sunlight. This impact may linger for up to six weeks. The hydrophobic version of the dye molecule was enclosed inside a porous nanoparticle to avoid this negative effect. The dye remained confined inside the Ormosil nanoparticle and did not spread to other body parts. At the same time, its ability to generate oxygen was unaffected, and the pore size of roughly 1 nm allowed oxygen to diffuse out readily [26].

B. Tissue engineering

The surface of natural bone quite often contains about 100 nm across features. The body would attempt to reject an artificial bone implant if the surface was left smooth. Because of that smooth surface, fibrous tissue is likely to form on the implant surface. This layer limits the bone-implant contact, which might cause the implant to loosen and cause more inflammation. It was shown that adding nano-sized structures on the surface of a hip or knee prosthesis could lower the likelihood of rejection and stimulate the production of osteoblasts. The osteoblasts are the cells responsible for the growth of the bone matrix and are found on the advancing surface of the growing bone. Polymeric, ceramic, and, more recently, metal materials have been used to illustrate the effect of more than 90% of suspended human bone cells attached to the nanostructured metal surface [27]. Finally, these findings would allow to design of more durable and longer-lasting hip or knee replacements and reduce the chances of the implant getting loose.

In orthopedics and dentistry, titanium is a well-known bone-repair substance. Fracture resistance, ductility, and weight-to-strength ratio are all high in this material. Unfortunately, it lacks bioactivity, making supporting cell adhesion and growth challenging. Bioactive apatite coatings are known to attach to the bones as a result, numerous procedures for producing an appetite coating on titanium have been used in the past. These coatings have a non-uniform thickness, weak adherence, and low mechanical strength.

Furthermore, a stable porous structure is required to support the nutrients transported through the cell growth. The use of a biomimetic approach is slow. The growth of apatite film with a nanostructure thus resulted in the formation of a highly adhesive substance, uniform nanoporous [24]. The layer comprised 60 nm crystallites with a stable nanoporous structure and bioactivity.

An artificial hybrid material was prepared from 15-18 nm ceramic nanoparticles and poly (methyl methacrylate) copolymer [28]. The human teeth viscoelastic behavior (healing) was demonstrated using the tribology approach. An investigated hybrid material, deposited as a coating on the tooth surface, improved scratch resistance and possessed a healing behavior similar to the tooth.

C. Multiplexed optical coding of biomolecules

Recent advances in analytical sciences and bioengineering led to the development of DNA chips, miniature biosensors, and microfluidic devices (such as micro-electromechanical systems). These enabling technologies have greatly influenced many areas of biomedical research. Research into genomics and proteomics is yielding more sequencing data. Technologies that can rapidly screen many nucleic acids and proteins are needed.

In various bio-tagging applications, single QDs of compound semiconductors have been effectively employed to substitute organic dyes [29]. This concept has been taken further by integrating different-sized QDs with varied luminous hues with polymeric microbeads [30]. Precise control of QD ratios has been achieved. The nanoparticles in those studies came in six colors and ten different strengths. It is enough to encode one million nucleic acid or protein sequences. The coding and target signals can be read simultaneously at the single-bead level, according to DNA hybridization research. Gene expression studies, high-throughput screening, and medical diagnostics will benefit from this spectral coding approach.

IV. THEORY

As an example of calculations, let us discuss a hybrid nano-system composed of spherical MNP of radius a , dielectric function ϵ_M and double QD (DQD) of disk shape with radii r_1, r_2 and dielectric constant ϵ_S . The distances between the center-to-center of the two particles is denoted by R , and their gap is d , respectively, as illustrated in Fig. 1 (a). There is no direct tunneling between the MNP and the DQD ($R > a > r_1, r_2$). The hybrid structure is embedded in a dielectric background with a dielectric constant ϵ_B and is subject to an electromagnetic field $E(t) = \frac{E_0}{2} e^{-i\omega t} + c.c.$ with ω is the carrier frequency, E_0 is the amplitude, and c.c. refers to the complex conjugate. Fig. 1 (b) shows the energy band scheme for the DQD system

with a wetting layer (WL). The plasmonic excitations of the MNP have a continuous spectrum; the excitations of the DQD are excitons with discrete energy levels. The DQD considered is composed of two QDs; each QD was an InAs QD with a disk shape of the radius of r and height of h . The sizes of the first QD are ($h = 0.1$ nm, $r = 3$ nm) while those of the second QD are ($h = 0.15$ nm, $r = 4$ nm). Each QD has one conduction and valence subband. The WL (InGaAs quantum well layer with 10 nm thickness) conduction and valence subbands are the reservoir states for both QDs. The interband transition $|1\rangle \leftrightarrow |3\rangle$ is excited by a strong coupling beam (frequency ω_p) with the Rabi frequency given by $\Omega_{03}^0 = \frac{E_{13}^0 \mu_{13}}{2\epsilon_{effs} \hbar}$ and a weak probe beam with a frequency ω_k drives the interband transition $|0\rangle \leftrightarrow |2\rangle$ and the Rabi frequency $\Omega_{02}^0 = \frac{E_{02}^0 \mu_{02}}{2\epsilon_{effs} \hbar}$ where μ_{13} and μ_{02} are the transition dipole moments of the DQD.

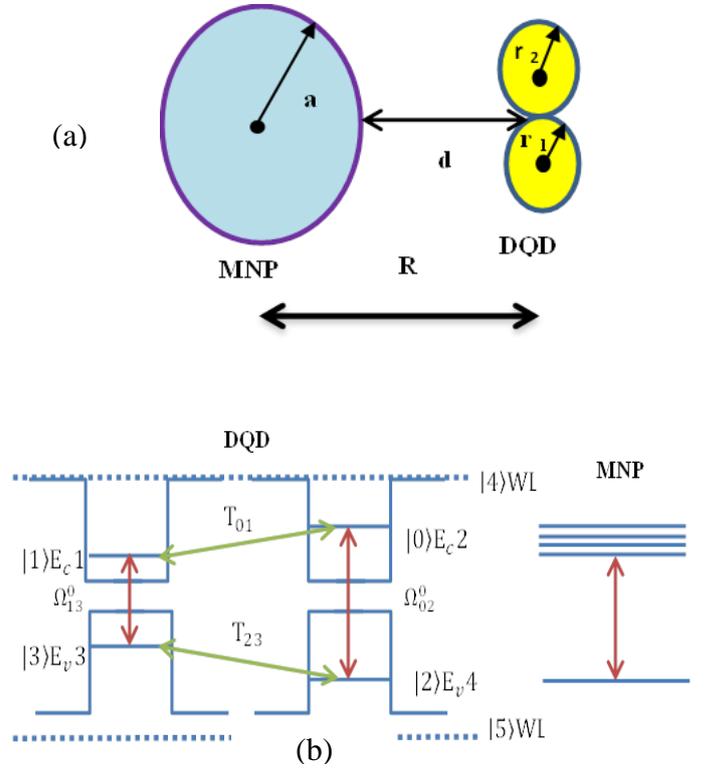


Fig. 1: (a) Scheme of a hybrid system composed of MNP and DQD; (b) The system's energy band structure; the arrows indicate the significant transitions.

The effective Rabi frequency $\Omega_{DQD,ij} = \mu E_{DQD,ij} / \hbar$ where $i \leftrightarrow j = 0 \leftrightarrow 2$ or $1 \leftrightarrow 3$ with $E_{DQD,ij}$ denotes the total electric field felt by the DQD, consisting of the externally applied field and the induced internal field from the MNP. It is given by [8],

$$E_{DQD,ij} = E_{effs,ij} + \frac{(4\pi\epsilon_B)\delta_\alpha\gamma a^3 E_{MNP,ij}}{\epsilon_{effs} R^3} \quad (1)$$

Where $\epsilon_{effs} = \frac{2\epsilon_B + \epsilon_S}{3\epsilon_B}$, $E_{effs,ij} = \frac{E_{ij}^0}{2\epsilon_{effs}}$, $\gamma = \frac{\epsilon_M(\omega) - \epsilon_B}{2\epsilon_B + \epsilon_M(\omega)}$, and $\delta_\alpha = 2$, since the applied fields are parallel to the interparticle axis (z -axis). ϵ_B is the background dielectric constant. The total field E_{MNP} acting on the MNP can be expressed as [16],

$$E_{\text{MNP},ij} = \varepsilon_{\text{effs}} \left(E_{\text{effs},ij} + \frac{1}{4\pi\varepsilon_{\text{B}}} \frac{\delta_{\alpha}\mu_{ij}}{\varepsilon_{\text{effs}}R^3} \rho_{ij} \right) \quad (2)$$

Using Eq. (2) in Eq. (1), we get,

$$E_{\text{DQD},ij} = E_{\text{effs},ij} \left(1 + \frac{\gamma a^3 \delta_{\alpha}}{R^3} + \frac{\gamma a^3 \delta_{\alpha}^2 \mu_{ij}}{2\pi\varepsilon_{\text{B}}\varepsilon_{\text{effs}}R^6} \rho_{ij} \right) \quad (3)$$

Hence, this results in the following effective Rabi frequency of the probe and pump fields,

$$\Omega_{ij} = \Omega_{ij}^0 \left(1 + \frac{\gamma a^3 \delta_{\alpha}}{R^3} + \frac{\gamma a^3 \delta_{\alpha}^2 \mu_{ij}}{4\pi\varepsilon_{\text{B}}\varepsilon_{\text{effs}}R^6} \rho_{ij} \right) \quad (4)$$

The linear susceptibility for the probe field, under the influence of the pump field, is given by [31],

$$\chi^{(1)} = \frac{2N_{\text{Q}}\mu_{02}^2}{\varepsilon_0\hbar\Omega_{02}} \rho_{02} \quad (5)$$

where N_{Q} is the number of DQDs per unit volume, ε_0 is the dielectric constant of vacuum, and the density matrix operator ρ_{20} is expressed as follows,

$$\rho_{20} = \frac{i(\gamma_0 + \gamma_1 + i\Delta_{10}) \left[\Omega_{02} \left(1 + \frac{\gamma a^3 \delta_{\alpha}}{R^3} \right) (\rho_{00} - \rho_{22}) + T_{32}\rho_{30} + \beta_{30}\rho_{23} - T_{10}\rho_{12} - \beta_{40}\rho_{24} \right] + i\beta_{21} [\Omega_{13}\rho_{30} - \beta_{30}\rho_{13}]}{(\gamma_0 + \gamma_2) + i[\Delta_{20} - \left(\frac{\gamma a^3 \delta_{\alpha}^2 \mu_{ij}}{4\pi\varepsilon_{\text{B}}\varepsilon_{\text{effs}}R^6} \Omega_{02} \right) (\rho_{00} - \rho_{22})]} \quad (6)$$

Where we take a small occupation as $\rho_{00} = \rho_{22} = 10^{-7}$ and also small interactions for $\rho_{30} = \rho_{13} = \rho_{23} = \rho_{12} = \rho_{42}$. The T_{01}, T_{32} are the tunneling components, γ_i is the relaxation rate from the state $|i\rangle$, Δ_{ij} is the detuning with $\Delta_{ij} = \omega_i - \omega_{ij}$ where ω_i is the resonant frequency of the i^{th} DQD state and ω_{ij} is the frequency difference between $|i\rangle$ and $|j\rangle$ DQD states, $\beta_{ij} = \frac{A_{ij}}{2} + \frac{1}{T_t}$ where $A_{ij} (= \frac{\mu_{ij}^2 \omega^2}{3\pi\hbar\varepsilon c^3})$ is the Einstein coefficient with T_t is the dipole dephasing time. Fig. 2 shows real and imaginary parts of MNP-DQD susceptibility at probe detuning. A high susceptibility results from the MNP polarization effect, which refers to the possibility of different uses for this structure. The susceptibility shift from zero detuning comes from the impact of MNP on the QD emission. The values obtained are in the range of our numerical model published recently [32].

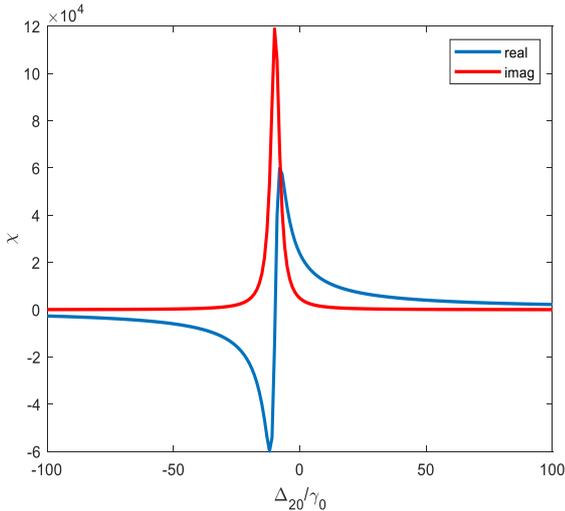


Fig. 2: Real and imaginary parts of MNP-DQD susceptibility at probe detuning.

V. CONCLUSIONS

This study modeled the real and imaginary parts of the MNP-DQD susceptibility under the pump-probe application. The effect of WL and the transition momenta for each DQD and WL-QD transition, which did not considered previously, are calculated. The hybrid DQD-MNP showed a high sensitivity indicating that this structure could be used in different fields.

Medication delivery focuses on the bulk of commercial nanoparticle uses in medicine. Nanoparticles replace organic dyes in biosciences applications that require excellent photostability and multiplexing abilities. There have been advancements in the direction and remote control of nano-probe functions, such as driving magnetic nanoparticles to the tumor and releasing the drug load or heating them to destroy the surrounding tissue. The main tendency in nanomaterial development is to make them multifunctional and programmable by external signals or the local environment, thereby transforming them into nano-devices.

To summarize, one of the biggest challenges in biomedical applications of nanoparticles lies in dealing with the issue of technology transfer. In this regard, for example, more interdisciplinary techniques are possible to ensure that laboratory-based research can more clearly mimic the predicted conditions found in vivo. There is also potential for significant contributions through mathematical modeling of complex systems to comprehend better the range of physical processes and consequences that jointly determine whether a given application will succeed.

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