Photothermal Characteristics Study of PEGylated Gold Nanorods

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Abstract

The present paper shows that gold nanorods were first synthesized and modified within different molecular weight of polyethyleneglycol ranging from 1000~5000. PEGylated nanorods were irritated and evaluated their photothermal effects. In order to achieve temperature optimization, we have also employed multi-wavelength laser diode system at various wavelengths (785 nm, 808 nm, and 852 nm) and power (100 mW~500 mW) to the target nanorods separately or combined for maximum hyperthermal effect. It is found that the highest temperature increase may be achieved by at certain wavelength combination near maximum absorption peak of nanorods than by single wavelength. This study will provide moderated rise of local temperature, and benefit further design of effective heating for hyperthermal therapy.

Keywords: gold nanorods, photothermal therapy, PEGylation

1. Introduction

Gold nanoparticles, aside from bulk metallic gold, have received great interest due to their remarkable size dependent optical, catalytic, and electronic properties. Rods like gold nanoparticles, in particularly, have high absorption at wavelength of Near IR section and sensitive surface plasmon resonance. Along with high efficiency photothermal conversion, gold nanorods have brought to great attention for the application in both cancer diagnosis and hyperthermia treatment. The use of gold nanoparticles for localized hyperthermia therapy was first revealed by Halas and coworkers. In their studies, NIR irradiation led to a rise of temperature for over 10℃ in the target area to destroyed the carcinomas and showed great tumor size reduction. Furthermore, El-Sayed et al reported in their work that with certain power of cw laser irritation applied , anti-EGFR antibody conjugated gold nanorods would cause photodestruction of 2 malignant oral epithelial cell lines. By changing the aspect ratio of nanorods, the absorption and scattering cross section can be tuned easily as well.

Though many results of photothermal therapy demonstrated the promising hyperthermia effect of damaging not only on cancer cell but also on bacteria, DNA and virus, however, the understandings of the relationship between nanoparticle parameter (surface modification, aspect ratio and concentration), laser specification (power, wavelength) and photothermal efficiency are still limited. Neither of them has been optimized to provide the maximum therapeutic effect that is crucial in photothermal tumor ablation.

Here in this work, we prepared non-cytotoxicity PEGylated gold nanorods grafted with different molecular weight of PEG ranging from 1000~5000 and evaluated their photothermal effect. With various intensity of applied laser power, temperature rise was discussed. Furthermore, single and combination wavelength laser irritation dependence of thermal efficiency is also demonstrated in this study. The ultimate goal is to develop correspond laser system for temperature controlled rising and optimum photothermal efficiency.

2. Experimental Design

2.1 Gold Nanorods Preparation

We employ the typical seed-mediated growth method with aid of surfactant and reducing agent described previously by El-Sayed et al. Basically, seed gold nanoparticles were first formed by adding hydrogen tetrachloroaurate (III) hydrate (0.01M, 250 Ul) to CTAB . Growth solution was prepared by adding ascorbic acid into solution containing $HAuCl_4$, Ag^+, and CTAB. Finally, the seed solution was rapidly mixed and solution colour changed to brown depending on seed size. The resulting solution of gold nanorods was centrifuged to remove the excessive surfactant and resuspended in water.

2.2 PEGylated Nanorods Preparation

mPEG- SH (Nanocs, MW= 1000, 2000, 5000) was added to the nanorods solution at final concentration of 5 mM. Rod was sonicated for 3 hours and centrifuged to remove surfactants and non specifically bound mPEG. The PEGylated nanorods were than re-dispersed in DI water and characterized using transmission electron microscopy. Absorption spectra of nanorods were also measured before and after PEGylation.

2.3 Photothermal Effect Characterizations

It is known that the absorption of nanorods depends on various parameters including the laser wavelength, beam spot size, laser power and the aspect (length/diameter ratio, "LWR") of the nanorods. For characterization of photothermal effect at various wavelength, a multiple wavelength diode laser (780-920 nm) integrated in a single device (controller) as shown in Figure 1 was developed. The diode lasers at various wavelength (with power of 100-500 mW each) could apply to the target nanorods separately or jointly. Direct measurement with fine needle thermocouple connected to the data recorder was used for data acquisition and further analysis.

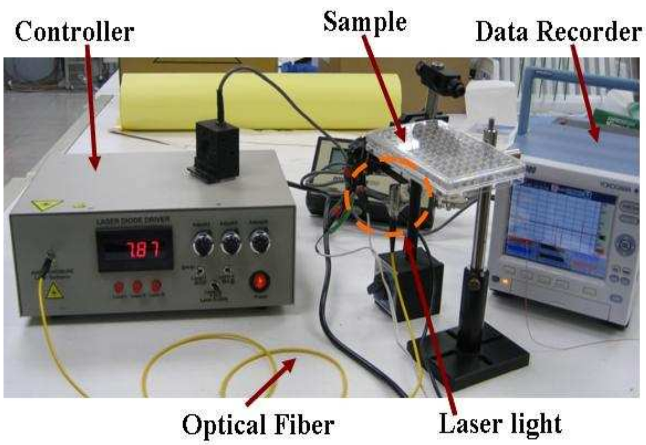

Figure 1: The experimental setup: Controller with multiple laser diode, along with optical fiber, sample holder, thermocouple and data recorder

3. Results and Discussion

3.1 Synthesis and Modification of Gold Nanorods

Near IR absorbing gold nanorods with length around 40 nm and diameter around 10 nm (estimate aspect ratio~4) resulting in an absorption peak at 760 nm~810nm were first fabricated. TEM study that shows in Figure 2 further confirm the narrow size and shape distributions without particles aggregation.

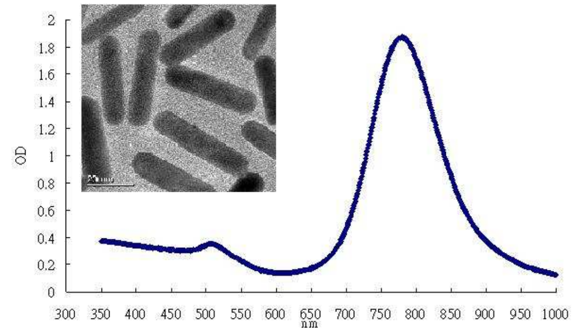

Figure 2. The UV/Vis absorption spectra and TEM image of seed mediated growth gold nanorods with absorption peak at 779 nm.

3.2 Characterization of PEGylated Nanorods

Due to gold nanorods stabilized with CTAB show strong cytotoxicity, PEGylation gold nanorods are necessary for medical application. Here in our studies, PEG_{1000}, PEG_{2000} and PEG_{5000} modified gold nanorods all showed a nearly neutral surface and little cytotoxicity using MTT assay (data not shown) which might be caused by unwashed CTAB in the NR solution. Absorption spectrums of gold nanorods were measured before and after PEGylation. Similar absorption spectrums that correspond to longitudinal and transverse oscillation modes were observed. TEM images and spectra shown in figure 3 both indicate that there's no particle aggregation of nanorods. It is also found that PEG_{1000} and PEG_{2000} modified nanorods have exactly same maximum absorption wavelength at 755 nm which point out that molecular weight of PEG has very little effect on shift of surface Plasmon mode.

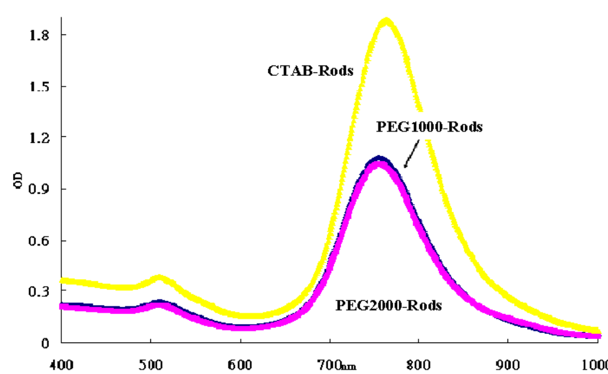

Figure 3. Absorption spectra of gold nanorods: Original gold nanorods covered with CTAB, PEG1000-modified gold nanorods and PEG2000-modified gold nanorods

3.3 Photothermal effect of PEGylated Nanorods

In order to evaluate photothermal responses of laser activated PEG-gold nanorods , 100 μl PEG_{1000} or PEG_{2000}

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-nanorods solution were added to 96 wells plate. Thermocouples were placed in the well and connected to data acquisition system. Glass coverslip was placed on the top of 96 wells to prevent evaporation of nanorods solution causing by local temperature increasing. The 785 nm laser light excitation with intensity controlled at 200 mW inserted from the bottom of the 96 wells.

Table 1 below shows characteristics and temperature profile of PEGylated nanorods with both PEG molecular weight=1000. Because of the limited options of laser diode, 785 nm, 200 mW laser excitation was applied for 240 sec, even though maximum absorption peaks of samples are at 755 nm. The temperature therefore increased slowly in the rate of 2.6 ℃ per minute. The different values of temperature increase of modified nanorods also identified factors thst might affect the photothermal efficiency. The particles concentration can be a major effect toward temperature response within same intensity of laser irritation. Within slightly changes (10 ppm) in concentration that is determinated by atomic absorption, the temperature increase change significantly under same irritation condition applied.

	PEG $_{1000}$-Rod-A	**PEG $_{1000}$-Rod-B**
Concentration (ppm)	**200.08**	**189.86**
Absorption Peak	**755 nm**	**755 nm**
Delta T (240 sec)	**10.2 ℃**	**8.0 ℃**

Table 1 Local temperature increased by laser irritation at 785 nm, 200 mW for 240 sec

3.4 Thermal Profiles Characterization of Single and Multiple Wavelength Laser Irritation

As mentioned in previous researches, rod shaped gold nanoparticles have stronger tunable surface plasmon absorption and better photothermal efficiency than spherical particles do. However, the heating effect only becomes especially strong under the Plasmon resonance conditions when the incident photon is close to the Plasmon frequency of nanorods. Owing to limited choices of irritation wavelength, the heating effect weakens easily. For example, rods which maximum absorption are at 755 nm and 779 nm (same concentration) were both irritated by 785 nm laser light, 200 Mw. It is shown in figure 4 that temperature of Au rods$_{-779nm}$ solution increased more rapidly (4.3 ℃ per min) than Au rods$_{-755nm}$ did.

Figure 4 also demonstrates temperature change versus times with various intensities of laser power applied on rods. It reveals that with the higher power intensity applied, the greater temperature increase was obtained.

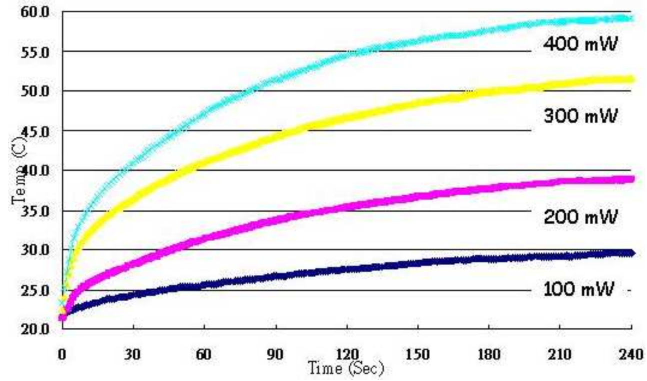

Figure 4 The temperature response of laser irritation on nanorods with various power ranging from 100 to 400 mW (maximum absorption peak at 779 nm)

We also observed the temperature response of laser irritation on nanorods with various wavelengths applied. As shown in Figure 5, the sample of 1mM Au rods$_{-779nm}$ solution were irradiated for 240 sec by single 785 nm laser (300 mW) and dual wavelength 785/808 nm laser (150/150 nm). We found out that the higher temperature increase can be achieved by at 785/808 nm wavelength combination near maximum absorption peak of nanorods. On the other hand, sample that is irritated by single wavelength (785 nm, 300 mW) has slower heating rate. This effect of irritating can be due to nanorods size distribution and relatively high absorption at 808 nm region. Although TEM images shows uniform nanorods with similar size, absorption spectra is very sensitive to the aspect ratio and most absorption of rods are ranging from 775 to 810 nm. After sample were exposed to 785/808 nm laser, more nanorods can be irritated and resulting greater temperature change.

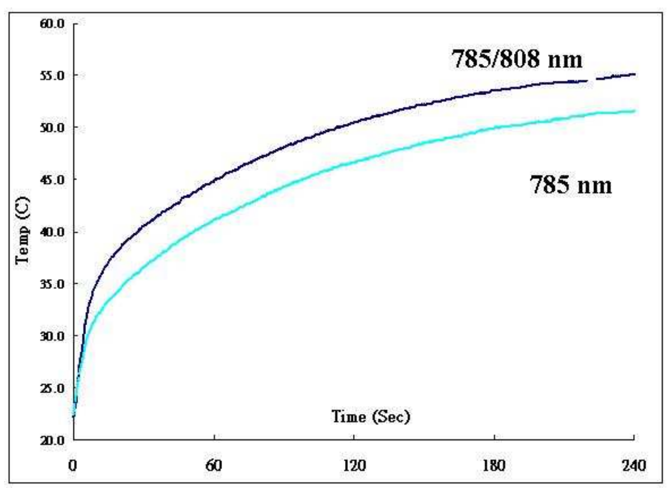

Figure 5 The temperature response of laser irritation on nanorods with various wavelength (maximum absorption peak of rods at 779 nm)

4. Conclusion

To conclude, we performed a series studies of photothermal responses from near IR irritated Au nanorods using integrated multiple wavelength diode laser system and data acquisition system. Nanorods modified with different PEG molecular weight ranging from 1000 to 5000 were synthesized successfully without aggregation. By observing the shift of absorption peak and temperature response after exposed to laser, we found that the photothermal properties are nearly the same between PEG_{1000}-Rod and PEG_{2000}-Rod. However, within slightly change in concentration of nanorods might cause an increase of temperature significantly.

In this study, we also demonstrated that with gradually increasing power, heat generated faster. We also achieve heating efficiency in combining various wavelengths (785 nm, 808 nm). With dual wavelengths applied, more nanorods at different aspect ratio could be irritated and therefore reaching higher temperature at same period of time. Our finding provides the first step for moderated rise of local temperature, and it will benefit further design of effective heating for hyperthermal therapy.

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