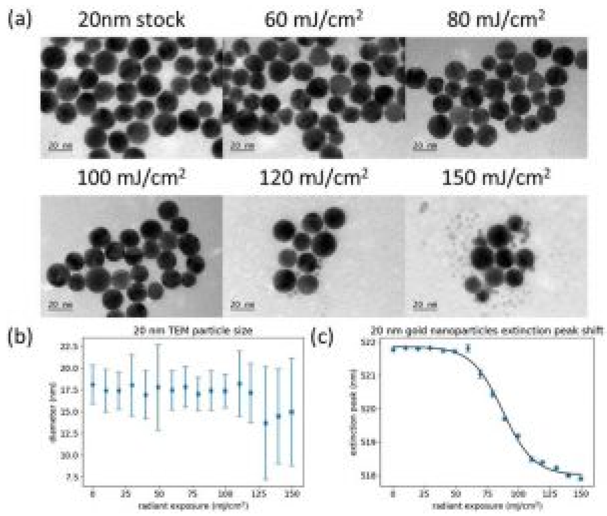
Quantitative Evaluation of Nanosecond Pulsed Laser-Induced Photomodification of Plasmonic Gold Nanoparticles



Biophotonic application of plasmonic gold nanoparticles has become a highly active field of research in recent years due to their unique chemical and physical properties, such as high absorption cross sections and spectral tunability[1]. Many of the unique properties of gold nanoparticles are governed by the surface plasmon resonance (SPR) effect, a collective oscillation of electrons on the nanoparticle surface that occurs when excited with light at an appropriate wavelength. The SPR results in a strongly enhanced electromagnetic field near the particle surface, which causes unique, shape- and material-dependent spectral variations in light absorption and scattering. These properties allow nanoparticles to be used not only as therapeutic agents[2,3,4], but also for diagnostic imaging[5,6]. The therapeutic effects produced by laser-nanoparticle interaction can occur through a variety of mechanisms. Photothermal transduction causes rapid heating in a localized area around the irradiated nanoparticles and has been used for the treatment of solid tumors *in vivo*, with both continuous-wave and nanosecond-pulsed lasers[7,8,9]. Photomechanical effects, such as cavitation, can occur when exposing plasmonic nanoparticles to pulsed laser light (nanosecond-to-femtosecond), and the resultant bubbles are capable of disrupting cancer cell membranes[10,11,12]. Photochemical effects, like the production of reactive oxygen species, have also been observed from laser irradiation of gold nanoparticles, with pulsed lasers having a greater effect than continuous-wave lasers[13,14]. The properties that make gold nanoparticles so effective for laser-based therapeutics can also lead to unintended side-effects in diagnostic procedures.

One of the most promising diagnostic techniques that may employ gold nanoparticle contrast agents is photoacoustic imaging (PAI), a rapidly maturing biomedical modality capable of macro- and micro-scale imaging[5]. In PAI, tissue is illuminated with a nanosecond pulsed laser, typically a Q-switched Nd:YAG with pulse duration in the range of 5–10 ns, at exposures below standard safety limits[15]. This exposure causes rapid optical absorption and thermal expansion that produces acoustic waves, which can be detected using an ultrasonic transducer. The use of gold nanoparticles as contrast agents for PAI has the potential to generate photothermal, photomechanical, or photochemical effects that result in tissue injury. Furthermore, the spectral changes brought about by nanoparticle photomodification can cause spectral shifts in absorption that degrade PAI-nanoparticle product performance[16].

While there are well-established laser safety standards for the skin and eye, these standards are insufficient when exogenous chromophores such as nanoparticles are present. Additionally, no standards exist for evaluating the performance of laser-nanoparticle combination products for medicine. In recent years, a number of studies have contributed knowledge on the laser-nanoparticle interaction processes and resultant bioeffects, as well as test methods that could form the basis of new standards. One key step in elucidating laser-nanoparticle interactions is to understand the photostability of nanoparticles and characterize laser induced photomodification processes, including photothermally-induced melting/reshaping effects that have been documented for different types of metallic nanoparticles[16,17,18,19,20,21,22]. they chose to study spherical gold nanoparticles as their surface plasmon resonance is close to the wavelength (532 nm) of the second-harmonic Q-switched Nd:YAG laser, which is broadly employed in biophotonics and photomedicine[23,24,25], and because these nanoparticles possess well-defined morphological properties and their spherical shape is well-suited for theoretical investigation.

Several prior studies have evaluated the effect of pulsed laser irradiation on gold nanospheres – more accurately gold “pseudospheres” since most of the particles studied, as well as commercially available versions, have faceted rather than smooth edges. One such study by Takami *et al*. looked at the size reduction of approximately 50 nm gold nanospheres at different pulse energies[18]. Werner *et al*. investigated the effect of irradiation wavelength on 55 nm gold nanospheres and was mostly concerned with modeling the difference between interband and intraband excitation[22]. Another study used dynamic light scattering (DLS), electron microscopy and UV-Vis spectroscopy to examine the impact of a single laser pulse on particles of different sizes[26]. While results were presented for a range of energy levels, specific damage thresholds were not determined and comparison with theoretical results was not presented. These prior studies have provided significant insights, yet are deficient in terms of generating a standardized test methodology as they either only used a single nanoparticle size or provided a qualitative description of the damage with no well-defined threshold.

Our overall objective was to facilitate the optimization of safety and effectiveness in emerging biophotonic products incorporating nanoparticles. Previous works have not established a common approach for assessing laser damage thresholds in nanoparticles, and information on the role of particle size in nanosphere damage is typically spread across multiple reports with inconsistent experimental conditions. Therefore, the goals of this proof-of-concept study were to implement and assess methodologies to quantitatively determine nanoparticle photomodification thresholds, and to generate data on the melting process and damage thresholds that can be used to improve understanding of this process. Specifically, we have conducted quantitative experimental and analytical investigation of the interaction between nanosecond laser pulses at 532 nm and plasmonic gold nanoparticles with diameters from 20 to 100 nm over a wide range of laser radiant exposures.

More information: Andrew M. Fales et al. Quantitative evalution of nanosecond pulsed laser-induced photomodification of plasmonic gold nanoparticles, Scientific Reports(2017). 10.1038/s41598-017-16052-7.