Light-Induced Release from Gold-Coated Liposomes

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ABSTRACT

We have computationally refined an experimental system with the potential for delivery and localized release of an encapsulated agent with high spatial and temporal resolution. We recently presented liposome-supported plasmon resonant gold nanoshells; in this composite structure, the liposome allows for the encapsulation of substances and the plasmon resonant structure facilitates rapid release of encapsulated contents upon laser light illumination. Using computational modeling, we now demonstrate that these liposome-supported nanoshells induce less local heating than solid gold spheres under optical trapping conditions, reducing their likelihood of damaging biological tissues used with this manipulation mechanism. We then present a general scheme for trapping of and localized release from gold-coated liposomes to enable accurate perturbation of cellular functions in response to released compounds, with possible applications in signalling pathways and drug discovery.

Keywords: nanoparticle, liposome, plasmon resonance, optical trapping, controlled release.

1 INTRODUCTION

Gold nanoparticles have found wide and varied use in applications in biology and nanotechnology, including detection and therapeutics. Furthermore, with regard to optical trapping, the use of gold nanoparticles has been shown to enhance trap stability relative to polystyrene beads [1], and can lead to improved trap sensitivity and particle detection. However, a major pitfall to the use of trapped gold nanoparticles in biological assays is substantial heating due to the absorption of gold, which can cause damage to biological samples [1]. Here we use computational modeling to demonstrate how our recently introduced composite material, gold-coated liposomes avoid dramatic sample heating when used with optical trapping while providing an additional functionality: the localized release of encapsulated compounds.

The gold-coated liposomes combine a thermosensitive lipid composition [2] with a shell-like assembly of gold nanoclusters that provide optical plasmon resonant properties similar to solid gold shells [3,4,5]. Expectedly, these composite nanoparticles exhibit the enhanced trapping stability thought to be associated with high polarizability of gold [6]. Also, the thermosensitive liposome in conjunction with a porous plasmon resonant coating allows for the encapsulation and release of compounds in response to specific light activation [3,4,5]. Release of compounds at a subcellular resolution allows for the tracking of individual cellular responses and cell-to-cell signaling [7]. In the case of cells that cannot be isolated with high purity, such as stem cells, this system might mitigate signal interference from progenitor cells and allow for monitoring the response of only cells of interest [8].

Here we demonstrate that liposome-supported gold shells induce less local heating than solid gold spheres containing equivalent amounts of gold. We also propose a trapping scheme that may enable the optical trapping of and subsequent localized release from gold-coated liposomes while avoiding heating of biological samples, to enable accurate assessment of cellular response to released compounds.

2 COMPUTATIONAL MODEL

To model the temperature distribution resulting from the optical trapping of solid gold sphere or liposome-supported gold shells, the heat equation was solved numerically in one dimensional spherical coordinates using FlexPDE:

\[
\text{div}(K \times \text{grad}(T)) + Q = c_p \times \frac{dT}{dt}
\]  

(1)

where \( T \) is the temperature change in K, \( K \) is the material thermal conductivity in W/nm×K, \( Q \) is the calculated laser power in W/nm³, and \( c_p \) is the material heat capacity in J/K×nm³. Solid gold spheres were modeled as spheres 28.8 nm in radius. Liposome-supported gold shells were modeled as an aqueous phosphate buffered saline (PBS) core 46 nm in radius, surrounded by a concentric lipid bilayer shell 4 nm in thickness and a gold shell 3 nm in thickness. For both particle types, the gold was modeled as the only point for heat absorption and the particles were surrounded by PBS. Boundary conditions were set at a radius of 10 µm from the center of the particle, and defined as \( \text{grad}(T)=0 \). The thermal conductivity and heat capacity values used are provided in Table 1.

Laser power values were estimated assuming a 0.8 µm diameter focused spot size for a 1064 nm TEM₀₀ laser operating at 100 mW. Laser pulses were modeled using square waves.
<table>
<thead>
<tr>
<th>Material</th>
<th>Thermal Conductivity W/nm·K</th>
<th>Heat Capacity J/K·nm³</th>
</tr>
</thead>
<tbody>
<tr>
<td>PBS</td>
<td>$6.0 \times 10^{-10}$</td>
<td>$4.180 \times 10^{-21}$</td>
</tr>
<tr>
<td>Lipid bilayer</td>
<td>$1.4 \times 10^{-10}$</td>
<td>$3.916 \times 10^{-21}$</td>
</tr>
<tr>
<td>Gold</td>
<td>$3.2 \times 10^{-7}$</td>
<td>$2.492 \times 10^{-21}$</td>
</tr>
</tbody>
</table>

Table 1: Thermal conductivity and heat capacity values used for materials in heat equation modeling. Values for PBS were taken from those of water and values for the lipid bilayer were taken from those of hexadecane [9].

3 RESULTS

Figure 1 demonstrates the resulting temperature distribution associated with optical trapping of a solid gold sphere and a liposome-supported gold shell using a continuous wave laser. As shown in Figure 1a, both the solid sphere and shell reach an almost equilibrium temperature after a few microseconds of light exposure, with the solid sphere reaching peak temperatures around 50% greater than that of the gold liposome. The temperature distributions as a function of radial distance from the particle centers is provided in Figure 1b. Both the solid sphere and the gold liposome have an even temperature distribution across their diameter, with the solid gold sphere reaching a higher particle temperature and having a steeper temperature gradient in proximity to its outer diameter. At distances greater than 150 nm from the particle centers, the two particle types appear to have equivalent temperature distributions. While gold liposomes reach lower peak temperatures, both particle types demonstrate considerable sample heating.

Figure 2 demonstrates how laser pulsing can be used in the optical trap configuration to both reduce sample heating and control the release of contents from gold-coated liposomes. A train of 100 ns pulses at a frequency of 1 MHz does not cause an increase in the baseline temperature of the particle, nor does it induce significant heating of the sample volume (Figures 2a and c). However, more rapid pulsing of 100 ns pulses at 5 MHz, leads to a significant and sustained increase in the baseline temperature of the particle (Figure 2b). But, as shown in Figure 2c, this sustained temperature increase at the particle is accompanied by only mild increases in the bulk sample temperature.

4 DISCUSSION

As shown in Figure 1, gold spheres trapped using a continuous wave laser reach peak temperatures about 50% greater than those of gold liposomes containing an equivalent amount of gold. These higher peak temperatures in solid gold spheres is echoed when using a pulsed trapping laser, as well (Figure 2). These dramatic temperature increases can cause damage to biological samples, including protein denaturation. Furthermore, the substantial heating of the bulk sample volume (Figure 1b) may skew cellular responses of interest by activation of heat shock signalling pathways.

The use of gold-coated liposomes in optical traps avoids heating that may cause biological sample damage. In addition, the gold-coated liposomes can encapsulate and release water soluble agents. When used in conjunction with optical trapping, they may enable localized release with sub-cellular resolution. As water-soluble agents require microseconds to milliseonds to transverse a thermosensitive liposomal membrane [10], a sustained increase in the baseline temperature of the gold-coated liposome is necessary for release to occur. Thus, specific laser pulsing schemes can be employed that prevent or promote increases in baseline temperature to selectively trap gold-coated liposomes or to release their content.
As shown in Figures 2a and b, a train of 100 ns pulses at a frequency of 1 MHz produces no baseline temperature increase, while a 5 MHz frequency induces a significant and sustained baseline temperature increase of about 5.3 °C over a period of 10 μs. As a result, the 1 MHz frequency pulse train enables stable trapping of gold liposomes without inducing release, while the 5 MHz pulse train may be used to release encapsulated contents with high spatial and temporal selectivity. While similar to photochemically caged compounds, the approach described here does not require chemical modifications of the delivered compounds, and many molecules may be released simultaneously without limitation of molecular size. Also, both pulsing schemes avoid large increases in bulk sample temperatures (Figure 2c) and thus diminish the detrimental effects of temperature changes on cellular processes under study.

5 CONCLUSIONS

In conclusion, we used computational modeling to demonstrate that gold-coated liposomes can be used in optical trapping studies involving biological samples with minimal sample heating and subsequent sample damage. We also demonstrated how pulsing of the trapping laser can be used to independently control the trapping of gold-coated liposomes and the release of their content, with high spatial and temporal selectivity. This type of functionality can be used in many cellular studies, including examination of signal propagation in neural networks and of stem cell response for the development of cancer therapies.

6 ACKNOWLEDGEMENT

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REFERENCES