Semiconductor resonant all-optical temperature sensor and thermal release trigger of encapsulated anti-cancer drugs for in vitro studies

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Abstract. Nanostructures made of high-index semiconductors (n > 2.5) with the several orders of magnitude lower losses than noble metals possess (Au, Ag, Pt etc.) are gaining high interest in recent years for various advanced optical applications, including nanothermometry and optical heating. Owing to the high-Q of Mie-optical modes that are being supported by the nanostructures, such nanoresonators can be considered as a powerful tool for light absorption at the nanoscale. However, high potential of resonant semiconductor nanoparticles in drug release and delivery applications has not been studied yet. In this work, we prove both experimentally and theoretically that optically resonant iron-oxide (III) (Fe₂O₃) can be employed as a remote optical trigger for thermal rupture of polymer microcontainers used as a drug delivery platform. Such approach allows one to measure real-time temperature via thermally sensitive Raman signal of iron-oxide nanoparticles, that were embedded into the walls of microcontainers. We believe that, suggested system consisting of resonant semiconductor nanoparticles and polymer carrier capsules can serve as a highly efficient drug delivery platform with controllable remote release with temperature feedback.

1. Introduction

Recent studies demonstrated considerable interest in plasmonic nanoparticles as nanoscale heat sources for different applications, including drug delivery. However, there are limitations with their applicability governed by either limited resonant performance or lack of direct thermometry at the nanoscale, suitable for real-time applications. Recently, it was discovered that non-plasmonic (dielectric and semiconductor) resonant nanoparticles are highly efficient light-to-heat energy converters in the visible and near-IR [1], making them attractive for numbers of bio-applications, including real-time tracing of protein unfolding process [2].

In this study, we reveal theoretically and prove experimentally novel approach concept for non-plasmonic effective optical heating and thermometry with resonant nanoparticles embedded into polymer drug carrier microcapsules walls for remote thermal rupture and subsequent release of the antitumor drug [3]. High-Q optical Mie-resonances, which occur upon laser illumination of the nanoresonators, are crucial not only for the enhanced absorption, but as well as for the enhanced thermally sensitive Raman signal [4], thus reducing the temperature measurement time.
2. Results and discussion.

We start our consideration from steady-state heat diffusion equation of a single spherical nanoparticle in homogeneous media illuminated by electromagnetic plane-wave. We believe that such approach is reasonable for optical heating of resonant nanoparticles in aqueous media (i.e. water, liquids for \textit{in vitro} studies).

The power absorbed by the nanoparticle of radius $a$ can be expressed in terms of the absorption cross section ($C_{\text{abs}}$) \cite{5} and the intensity of the incident radiation ($I$) \cite{6}:

$$ Q = C_{\text{abs}} I $$ \hspace{1cm} (1)

To determine the temperature distribution inside the particle $T_1(r)$ and outside $T_2(r)$, it is necessary to solve the heat diffusion equations:

$$ \nabla (\kappa_1(r) \nabla T_1(r)) = -q(r) $$
$$ \nabla (\kappa_2(r) \nabla T_2(r)) = 0 $$ \hspace{1cm} (2)

where $\kappa_1$ and $\kappa_2$ are the thermal conductivities of the particle and the environment, respectively, $q$ is the power density (in this case it is equal to $q = \frac{Q}{V} = \frac{3Q}{4\pi a^3}$). Assuming the thermal conductivities $\kappa_1$ and $\kappa_2$ are homogeneous in space, and taking into account the boundary conditions, the solutions of the equations are written in the form:

$$ T_1 = \frac{Q}{8\pi \kappa_1 a} \left( 1 - \frac{r^2}{a^2} \right) + \frac{Q}{4\pi \kappa_2 a} T_0 + T_0 $$ \hspace{1cm} (3)

$$ T_2 = \frac{Q}{4\pi \kappa_2 a} + T_0, $$

where $T_0$ is the medium temperature before excitation of the nanoparticle. Assuming that the thermal conductivity of the material of the particle is much larger than the thermal conductivity of the environment ($\kappa_1 \gg \kappa_2$), the temperature change of the nanoparticle will be:

$$ \Delta T = \frac{C_{\text{abs}} I}{4\pi \kappa_2 a} $$ \hspace{1cm} (4)

**Figure 1.** Optical heating of spherical iron-oxide nanoparticle in aqueous homogeneous media for different nanoparticles radii and incident wavelengths in visible and near-IR region. Incident wavelength was of 633 nm, 790 nm and 1000 nm. Considered intensity is 1 mW/µm$^2$. Calculation is done using eq.4.
Figure 1 depicts analytical calculation for optical heating of spherical semiconductor iron oxide (III) nanoparticles in homogeneous aqueous media using eq.4. The results demonstrate worsening of optical heating efficiency upon red-shifting of incident wavelength to the near-IR. However, optical heating remains sufficient even in the region of 1000 nm, thus making these nanoparticles promising for bio-medical application, since it corresponds to biological tissue transparency window. Moreover, spherical semiconductor nanoparticles with thermally sensitive Raman scattering already demonstrated the ability not only in light-to-heat conversion at nanoscale but also serving as nanothermometer [1].

On the other hand, polymer microcarriers attracted a lot of interest among scientist due to ability for remote targeted release of medical drugs [7]. In this work, we propose combining the ability for optical heating and thermometry of semiconductor nanoparticle and the carrier systems based on polyelectrolyte microcapsules. Thus, making drug delivery systems with remote thermally induced all-optical release trigger.

![Figure 2](image)

**Figure 2.** (A) Bright-field microscopy image of the fabricated microcapsule with iron oxide nanoparticles embedded into walls. Scale bar is 2µm. (B) Scanning electron microscopy (SEM) image of the fabricated polymer microcapsule with embedded into walls iron oxide nanoparticles. Scale bar is 2µm.

Figure 2 demonstrates images of fabricated microcapsules with iron-oxide nanoparticles embedded into walls carried out by means of optical elastic bright-field microscopy (Figure 2(A)) and scanning electron microscopy (Figure 2(B)). The nanoparticles under laser illumination serve both as temperature sensor and nanoheater for thermal rupture of the capsules wall.

Therefore, we believe that suggested approach of combining semiconductor resonant nanoparticles with active thermally sensitive Raman response and polyelectrolyte microcarriers of medical drugs can serve as an effective platform for number of bio-medical applications.

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**References**

[1] Zograf GP et al. 2017 *Nano Letters* 17(5) 2945-2952
[2] Milichko VA, Zuev DA, Baranov DG, Zograf GP et al. 2018 *Laser & Photonics Reviews* 12(1) 1700227
[3] Zograf GP et al. 2019 *Laser & Photonics Reviews* (under review)
[4] Dmitriev PA et al. 2016 *Nanoscale* 8(9) 5043-5048
[5] Bohren CF and Huffman DR 2008 *Absorption and scattering of light by small particles* (New York - John Wiley & Sons)

[6] Baffou G and Quidant R 2013 *Laser & Photonics Reviews* 7(2) 171-187

[7] Zyuzin MV et al. 2017 *Bioconjugate chemistry* 28(2) 556-564