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Heating of aqueous suspensions of silicon nanoparticles by a 808-nm diode laser for application in local photohyperthermia

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Abstract. **3D simulation of the distribution of thermal fields in aqueous suspensions of silicon nanoparticles upon irradiation by a high-power 808-nm laser diode operating in cw and quasi-cw repetitively pulsed regimes is performed. It is shown that irradiation by a repetitively pulsed laser with a peak power of 10 W and a pulse duration of 300 ms can form a region with a maximum temperature exceeding 42 °C, which is promising for application in cancer photohyperthermia for local heating of biotissues at a given depth.**

Keywords: *high-power diode laser, silicon nanoparticles, hyperthermia.*

1. Introduction

In recent years, solid nanoparticles (NPs), which have unique structural and physicochemical properties, have attracted increasing attention because they can be used for solving the problems of biological imaging [1], therapy [2], and biosensorics [3]. Nanoparticles based on chemically pure silicon (Si) are an example of low-toxic nanomaterials biodegradable in biological tissues with formation of orthosilicic acid, which is naturally removed from the organism [4, 5]. The unique optical properties of silicon NPs and nanocrystals [6] open wide possibilities for their biophotonic applications for imaging cells and tissues [7, 8], in particular, for nonlinear optical 3D biological imaging [9]. Nanoparticles based on crystalline and porous Si can be used for delivery of drugs [7, 10], as well as in photodynamic [11] and sonodynamic [12] therapy. Extensive studies are performed on the use of porous silicon NPs as photohyperthermia agents and for thermally controlled drug release in cancer therapy [13, 14].

The principle of photohyperthermia consists in the transformation of optical radiation absorbed by tissues into heat, which, at a sufficiently high temperature, destroys cancer cells. It is known that Si NPs from 10 to 100 nm in size, which rather well absorb light in the visible and near-IR spectral regions [6], can accumulate in the tumour region near cell membranes and penetrate into cells [7–9]. It was found that the optical radiation energy absorbed by NPs transforms into heat, which leads to thermal destruction of cancer cells in the region of localisation of NPs [15]. Large-scale implementation of photohyperthermia in medical practice was accelerated by the use of reliable, inexpensive, and compact light sources based on high-power single laser diodes emitting in the spectral range of 800–808 nm, i.e., in the transparency window of biotissues [16–19]. For these sources, quasi-cw (QCW) and pulsed regimes were developed and the problems of reliability, simple design, and inexpensive power supply and cooling systems were solved [20]. However, in the case of photohyperthermia under cw irradiation, there exists a risk of damaging healthy tissues surrounding the tumour, which restricts the application of this method.

To increase the photohyperthermia efficiency and safety, is seems promising to use a repetitively pulsed irradiation regime, which prevents a significant increase in the average temperature of the tissue. In this case, due to selective absorption of energy by NPs, the local temperature in the irradiated region may exceed 42 °C, which is sufficient for thermal destruction of unhealthy biotissues and cells. The use of Si NPs with diameters of 20–50 nm and concentrations from 0.1 to 1 g L^{-1} for spatially localised pulsed photohyperthermia with the use of cw or repetitively pulsed radiation at a wavelength λ = 808 nm was studied in [16]. In this work, the authors observed that the photohyperthermic destruction of unicellular organisms is stronger in the case of excitation of NPs by repetitively pulsed radiation with a pulse duration of hundreds of milliseconds. However, to understand the results obtained in [16], especially in the case of a repetitively pulsed regime, it is necessary to perform theoretical analysis of photo-heating of Si NPs in aqueous suspensions.

In the present work, we theoretically study heating of aqueous suspensions of Si NPs under action of cw and repetitively pulsed laser radiation with a wavelength of 808 nm in order to find regimes for spatial and temporal localisation of hyperthermia for biomedical purposes.

2. Experimental model and method

To model the heat release resulting from light absorption by Si NPs dispersed in water, we used the ComSol Multiphysics software to numerically solve the heat conduction equation, which can be written in the form

$$\frac{\partial T}{\partial t} = D\nabla^2 T + \frac{H}{\rho c}, \quad (1)$$

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where T is the temperature, t is the time, $D = 1.43 \times 10^{-7}$ m s^{-1} is the thermal diffusivity (temperature conductivity) of water, $c = 4.2$ J g^{-1} K^{-1} is the thermal capacity of water, $\rho = 1$ g cm^{-3} is the water density, and H is the heat source function.

When aqueous suspensions of NPs are irradiated by laser pulses with a duration of hundreds of milliseconds, it is necessary to take into account that, on the one hand, the heat diffusion length in water for 100 ms is $\sim$100 μm, which is an acceptable accuracy for localised hyperthermic destruction of tumours. On the other hand, at such a long pulse duration, it is not necessary to consider each NP as an individual heat source, but it is possible to calculate the integral effect of the entire ensemble of NPs in suspension under the condition that the temperature distribution profile is uniform on the scale of the distance between NPs.

The geometrical parameters of a laser beam in the NP suspension in the considered model were given in the form of an inverted truncated cone (Fig. 1) with geometrical dimensions corresponding to the experimental conditions of [16], in particular, to the 0.5-mm diameter of the laser spot at the entrance to the cuvette and the divergence angle of 10°.

For calculations, we used the following boundary conditions: the temperature of the external water surface and all the cuvette walls is constant and equal to 22.5 °C, which corresponds to the experimental conditions. Note that the thermal conductivity and thermal capacity of the plastic cuvette

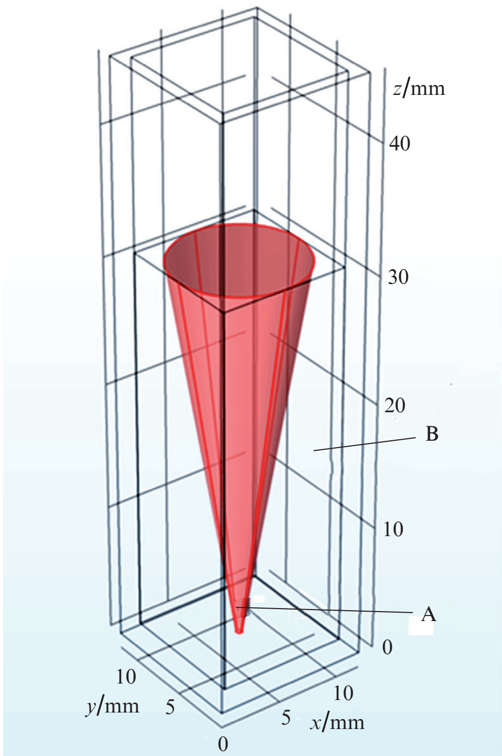

Figure 1. Schematic of the considered problem of photoinduced heating of a liquid with dispersed Si NPs in a transparent cuvette with a square cross section 10 × 10 mm with a heat source in the form of a truncated cone (dark region).The temperature on the cuvette walls and over the liquid surface is taken constant. A and B are the points on the beam axis with coordinate $z = 2$ mm and outside the photoexcitation region with $z = 10$ mm, respectively, which are used for detailed analysis of the temperature kinetic.

material (polystyrene) were used as the parameters of the calculation model. The heat release function depends on time and the z coordinate, whose zero value lied in the plane of the truncated cone vertex, which, under the experimental conditions, approximately corresponded to the position of the focused laser beam at the entrance to the cuvette. The change in the intensity of the laser beam propagating along the z direction can be described by the Bouguer – Lambert – Beer law

$$\frac{\mathrm{d}I}{\mathrm{d}z} = -I_0 k \exp(-kz), \tag{2}$$

where I_0 is the initial laser radiation intensity and k is the light absorption coefficient.

The heat source function is found from expression (2) with the opposite sign taking into account the beam divergence (see Fig. 1) multiplied by the dimensionless function of the temporal profile of the laser radiation intensity $M(t)$,

$$H(z,t) = I_0 \frac{S_0}{S(z)} M(t) k \exp(-kz), \tag{3}$$

where S_0 and $S(z)$ are the laser beam cross sections at the entrance to the cuvette with the NP suspension and at a point with coordinate z. In the case of the repetitively pulsed regime, function $M(t)$ was given according to the experimental conditions of [16] by a rectangular periodic function with a ratio between the pulse duration and the interpulse time of 3 : 7 at a pulse repetition rate of 1 Hz.

Note that the used model does not take into account light scattering from NPs, which is justified for their average sizes of $\sim$10 nm typical, for example, for NPs obtained by femtosecond laser ablation/fragmentation or plasmochemical synthesis [9, 16]. At the same time, for larger Si NPs formed, for example, by picosecond laser ablation or mechanical grinding of porous silicon layers [21], light scattering obviously should be taken into account when analysing the laser beam propagation and heat release caused by this propagation.

The 3D simulation of heating of aqueous suspensions of Si NPs and, for comparison, of distilled water was performed for cw and quasi-cw repetitively pulsed irradiation regimes. The average laser power in the quasi-cw regime was identical to the power in the case of cw irradiation. For example, the quasi-cw regime with a power of 10 W and a duty cycle of 30% (pulse duration 0.3 s, interval 0.7 s) was compared with the 3-W cw regime. Note that the powers in the cw and quasi-cw regimes were chosen to provide the required heating of the medium.

In calculations, the absorption coefficient of light with $\lambda = 808$ nm in water was taken to be 0.02 cm^{-1} [22], while the absorption coefficient for aqueous suspensions of Si NPs was determined experimentally and depended on the NP concentration. We studied aqueous suspensions of Si NPs obtained by plasmochemical synthesis (ACS Materials, United States) with average sizes of 15 nm and a concentration of 0.4 g L^{-1}, which is close to NPs studied in [16] and to NPs obtained by femtosecond laser ablation/fragmentation of silicon targets in water [9]. The light absorption coefficient in a suspension of Si NPs was estimated measuring the power of an 808-nm laser diode radiation passed through a plastic cuvette similar to the cuvette shown in the Fig. 1 and filled with the studied suspension. The measurements were performed using a wide-aperture pyroelectric power meter with an UP25N-40S-H9-D0 measuring head and a SOLO-PE monitor (Gentec, Canada). The measurement results taking into account losses for reflection from the cuvette walls and the cuvette–water interface allowed us to estimate the absorption coefficient, which turned out to be proportional to the concentration of NPs in the studied range 0.1–1 g L^{-1} and equal to 0.20 ± 0.01 cm^{-1} for a Si NP concentration of 0.4 g L^{-1}.

According to the above-described model, for experimental verification of the calculated thermal fields, we irradiated the suspensions of Si NPs by a laser diode (λ = 808 nm) [16–20] from the cuvette bottom and measured the temperature by a TMTsP-1 digital medical thermometer (MIREA, Russia) with a tiny temperature sensor (1 × 2 mm) (Exacon Scientific, Denmark) with a measuring range of 5–50 °C, a measurement error of 0.01 °C, and a discretisation frequency of 15 Hz. The temperature sensor was placed into the peripheral region of the cuvette (point B in Fig. 1) to minimise the influence on the laser beam propagation.

3. Calculation results and discussion

The calculation results (Fig. 2a) show that cw irradiation for 5 min leads to the formation of a region of increased temperature reaching its maximum (28 °C) in the region lying 1–2 mm above the cuvette bottom (point A in Fig. 1). At the same time, at the instant of the quasi-cw laser pulse termination, the maximum temperature increases to 29 °C and the size of the heated region noticeably increases (Fig. 2b). This effect can be explained by a low thermal conductivity of water, which slows down the heat removal from the region of the laser radiation absorption to the cuvette walls, whose outer surfaces, according to the chosen boundary conditions, have a fixed temperature.

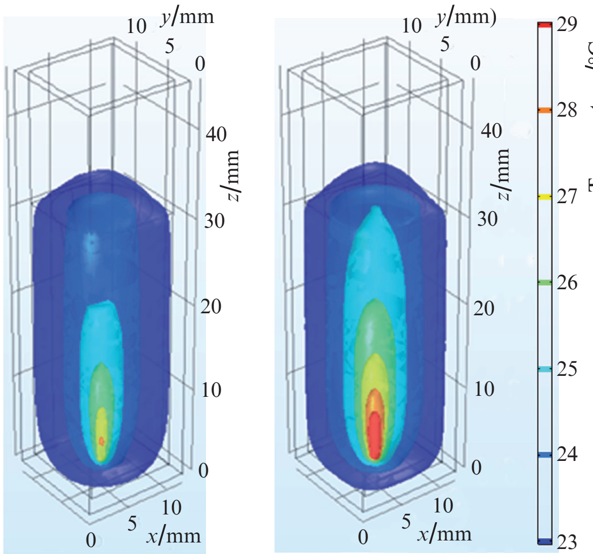

Figure 2. (Colour online) Isothermal surfaces in a cuvette with water (k = 0.02 cm^{-1}) irradiated for 5 min in (a) a cw regime with a power of 3 W and (b) a quasi-cw regime with a peak power of 10 W and a duty cycle of 30 % at the instant of pulse termination.

Figure 3 presents the simulation results for a suspension of Si NPs with a concentration of 0.4 g L^{-1}, which corresponds to the data of [16]. One can see that, after irradiation for 5 min, the temperature in the hottest region can exceed 70 °C, which is considerably higher than in the case of pure water (see Fig. 2). In the case of NPs, the region with a temperature exceeding 40 °C occupies a considerable part of the liquid volume, and, in addition, this part upon irradiation in the quasi-cw regime (Fig. 3b) is considerably larger than upon cw irradiation (Fig. 3a). These results allow one to understand the experimental data on more effective hyperthermic destruction of cells under repetitively pulsed laser radiation with a wavelength of 808 nm in the presence of silicon NPs [16].

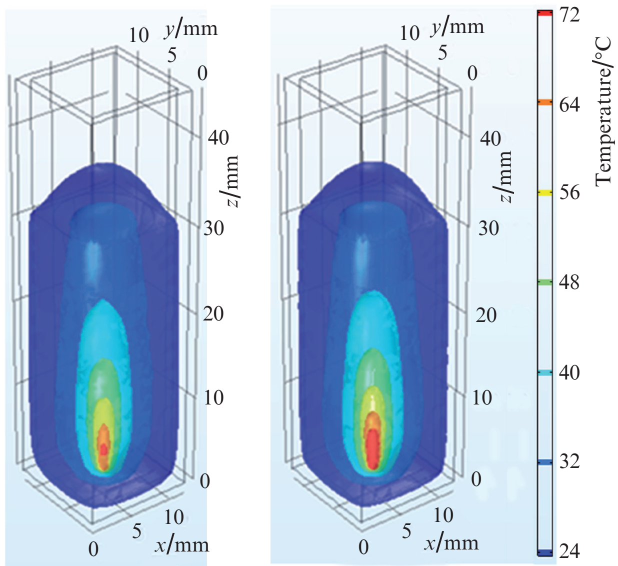

Figure 3. (Colour online) Isothermal surfaces in a cuvette with an aqueous suspension of Si NPs (k = 0.2 cm^{-1}) irradiated for 5 min in (a) a cw regime with a power of 3 W and (b) a quasi-cw regime with a peak power of 10 W and a duty cycle of 30 % at the instant of pulse termination.

Figure 4a shows the calculated dependences of the temperature of an NP aqueous suspension at the initial period of laser irradiation for the region with the maximum temperature (point A in Fig. 1) and for the heat sensor location (point B in Fig. 1). The obtained experimental data for the same instant of laser irradiation are shown in Fig. 4b. One can see from Fig. 4a that the maximum temperature can exceed 42 °C even 5 min after the start of irradiation in the cw regime and may reach 50 °C during the action of a laser pulse in the quasi-cw regime. The experimental dependences of photoinduced heating shown in Fg. 4b well agree with the simulation results for both regimes. The quantitative differences between the calculated and experimental data can be related to a finite accuracy of determination of the heat sensor location, as well as to the use of the simplified model which does not take into account convection processes and evaporation from the liquid surface. Note that the allowance for convection in the model may probably lead to a better agreement with experimental results. However, our measurements of temperature during irradiation with the use of a contactless thermometer

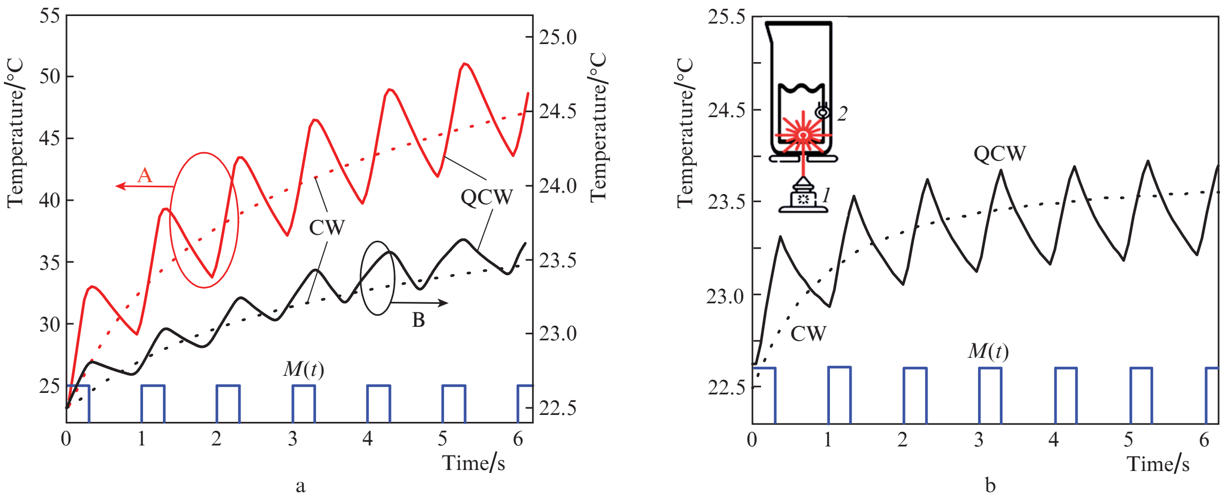

Figure 4. (a) Calculated dependences of temperature in the regions of maximum heating (point A) and the heat sensor location (point B) in a cuvette with an aqueous suspension of Si NPs (0.4 g L^{-1}) under irradiation in a cw regime (dotted curves) and a quasi-cw regime with a duty cycle of 30% (solid curves) and (b) experimental dependences of temperature at point B under irradiation in the same regimes [the inset shows the experimental scheme: (*1*) laser and (*2*) heat sensor]. The time dependence of the laser pulse intensity $M(t)$ in the quasi-cw regime is shown by the series of rectangular pulses.

showed that the increase in the temperature of the cuvette walls is insignificant and lie within the measurement error (±0.1 °C). Therefore, within the studied ranges of temperature fields, the heat transfer to the walls due to convection can be neglected.

The obtained results indicate that the quasi-cw irradiation regime is advantageous for enhancement and localisation of photohyperthermia caused by absorption of light by Si NPs. Indeed, the temperature of protein coagulation and cell death is taken to be 42 °C, which is achieved with local heating by 5–6 °C from the initial temperature of 37 °C. In this connection, the possibility of achieving a much higher temperature upon photoexcitation in the presence of Si NPs, especially in the quasi-cw regime, which was predicted by the model, seems very promising for photohyperthermia. Unfortunately, biotissues, in contrast to the studied aqueous suspension of NPs, exhibit both strong light scattering and intense heat removal due to blood circulation, which makes it more difficult to achieve photohyperthermia. One of the ways to increase the photoheating efficiency is to increase the concentration of Si NPs, which, however, is problematic in the case of systematic (intravenous) injection. Note that the silicon concentration of 0.4 g L^{-1} chosen in our work corresponds to harmless levels for *in vitro* and *in vivo* applications of NPs both based on porous silicon [11–13] and obtained by laser ablation [8, 9, 23].

4. Conclusions

The 3D temperature distributions obtained upon irradiation of aqueous suspensions of Si NPs by a laser diode with a wavelength of 808 nm, which lies in the range of the transparency window of biological tissues, indicate that it is possible to achieve spatially localised hyperthermia using relatively low radiation powers and harmless concentrations of nanoparticles. It is found that, using laser irradiation with a power of 10 W in a repetitively pulsed regime with a pulse duration of tenths of a second, it is possible to form a local region with a temperature considerably exceeding 40 °C, which allows one to perform hyperthermic treatment of biotissues. The obtained results demonstrate the potential advantage of a repetitively pulsed laser diode regime compared to a cw regime and can be helpful for developing new methods of local photohyperthermia of tumours with minimal heating of the surrounding healthy tissues.

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