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In silico study of thermal field distribution in cell culture media irradiated with wavelengths of singlet oxygen generation

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ABSTRACT

The interaction of laser radiation of wavelengths of direct optical generation of singlet oxygen with cell culture media was simulated. Using the COMSOL Multiphysics software, the distribution of the thermal field over the culture media volume was obtained depending on the wavelength, power and exposure time. The results demonstrate the importance of taking temperature into account when conducting experimental studies at the cellular and organismal levels.

Keywords: singlet oxygen, direct optical generation, thermal field.

1. INTRODUCTION

Oxygen and its partially reduced chemical products, known as reactive oxygen species (ROS), have important regulatory and signaling functions.[1] The basic triplet state of oxygen has several absorption bands in the infrared and visible regions (optical range between 1300 nm and 390 nm), at which singlet oxygen ($^1O_2$, one of the major ROS) can be produced.[2] Photon absorption in the particular absorption wavelengths corresponding to different electronic-vibrational molecular levels leads to excitation of the specific $^1O_2$ state. The possibility of direct excitation of an oxygen molecule by light in the ground triplet state ($^3O_2$) and regulation of its production by changing the light intensity and exposure time is of undoubted interest for fundamental and practical medicine. 1270 nm, 1065 nm, 760 nm bands have found the greatest application for the direct generation of $^1O_2$.[3–6]

The recent research results using direct excitation of oxygen are aimed at studying the initiation of oxidative stress caused by exposure to laser radiation and destabilization of cell metabolism after the end of the effect,[7] of induction of tumor cell death,[8] as well as at establishing the relationship between the dose of laser exposure and cell death.[9] It was found that the generation of singlet oxygen induced by different doses of laser radiation can also act as an activator of mitochondrial respiration and ATP production in the brain.[10]

Despite the growing interest, the main drawback of direct generation of $^1O_2$ is the low light absorption of molecular oxygen. It can be compensated by changes in light intensity and exposure time.[11] Wide possibilities to control these parameters of laser radiation allow for different effects on biological tissues. However, the increase in the radiation power of laser can induce a local temperature increase around the laser spot.[12] Although absorption by H_2O is relatively low below 1300 nm and significantly decreases in the region of spectrum from 950 nm and below,[13] the increase in radiation power and heat transfer to the immediate environment could produce significant local thermal effects around the laser spot.[12] This may be critical considering the temperature governs every biological reaction within living cells, in particular, the temperature increase can induce cytotoxic effects or cell death.

To select the optimal ratio of laser radiation parameters and exposure time for subsequent research and to identify the effect of optical dose-dependent generation of singlet oxygen on the analyzed processes, *in silico* studies of the interaction of optical radiation of various wavelengths of direct optical generation of singlet oxygen and modeling of thermal effects were carried out. The cell culture media (CCM) in the coverslip cell chamber was considered as analyzed objects.

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2. MATERIAL AND METHODS

Heat generation is determined by the optical properties of the media and laser parameters. They are primarily the irradiance, irradiation time, and absorption and scattering coefficients. These coefficients itself are a function of the laser wavelength. Heat transport is solely characterised by the thermal properties of the media such as heat conductivity and heat capacity. In this study, the heat transfer equation and related boundary conditions were numerically simulated using a finite element solver, COMSOL Multiphysics software (COMSOL Inc., Burlington, USA).

The temperature distribution was calculated by combining the Beer-Lambert law (Eq. 2) with the heat transfer equation:

$$\rho C_p \frac{\partial_T}{\partial_t} = \nabla \cdot (k\nabla) + Q_{laser}, \tag{1}$$

The laser beam intensity is determined using the Beer-Lambert Law. As the beam is absorbed, it deposits energy which acts as a heat source.

$$Q_{laser} = \mu_a I_0 e^{-\mu_a \cdot z}, \tag{2}$$

where μ_a is the absorption coefficient of the tissue (1/cm); I_0 is the irradiation intensity at the tissue surface (W/m^2); z is the depth of tissue.

The properties of water were used as thermal and optical characteristics of CCM. The effective attenuation of water is formed by the absorption coefficient when the scattering coefficient in the NIR region tends to zero.[13] Information from the COMSOL libraries[14] and a following resource[15] were used to determine the thermal properties of the models.

A standard coverslip cell chamber with 2 mm of water are heated by a laser in CW mode. For modeling, the domains are meshed using a triangle swept mesh. The power of the laser radiation varies by 50–250 mW with a step of 50 mW. The laser beam is modeled as a heat source in the plane with Gaussian profile with σ = 1.7 mm. It was supposed that the laser irradiates the water perpendicularly. The exposure time is 10 min. The calculations were carried out for the following wavelengths: 760 nm, 1064 nm and 1267 nm. The initial temperature was assumed to be uniform at 22 °C (295.15 K).

3. RESULTS AND DISCUSSION

Fig. 1a-c show the heat distribution in coverslip cell chamber volume and surface temperature distribution for three wavelengths at a laser power of 250 mW. Fig. 1d-f demonstrate the dependence of temperature on the coverslip surface with time.

The temperature rapidly increased in the early stage and gradually rose up afterwards and finally approached a steady-state value. The maximum heating of the coverslip surface reaches 30.1 °C at 1267 nm. The results show that for 760 nm, every 50 mW of radiation increases the temperature by about 0.05 °C, for 1064 nm by 0.23 °C, for 1267 nm by 1.6 °C. Such a large difference in heating is due to an order of magnitude difference in the water absorption coefficient at 1267 nm, compared to the other two wavelengths.

The simulation results obtained in this work are of great value in the context of the significant influence exerted by temperature on the chemical and biochemical reactions in living organisms. Heat increases kinetic energy in cells by speeding up the molecules involved in chemical reactions. In general, the effect of temperature on the rate of biological processes can be described using the Arrhenius equation. At the same time, this effect can be a more complex and multistep process, such as aerobic metabolism, that relies on mechanisms acting across multiple levels of biological organization.[16]

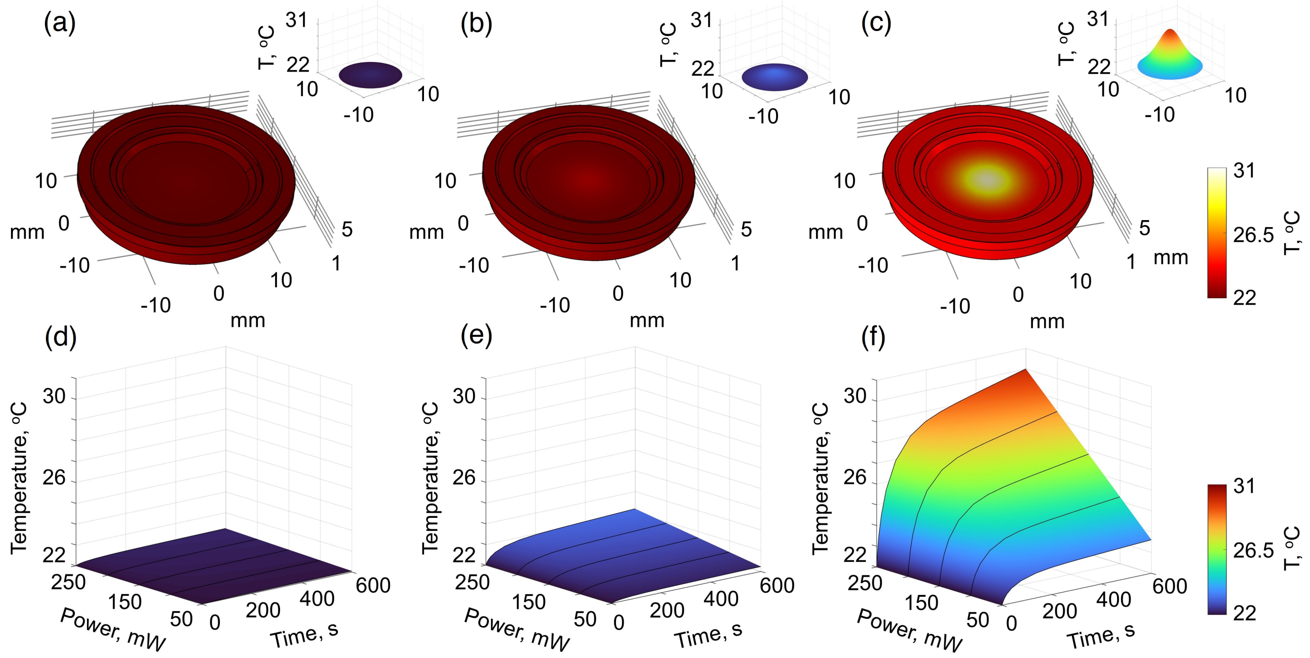

Figure 1. Temperature distribution in the water after (a) 760nm, (b) 1064 nm and (c) 1270 nm laser irradiation with power of 250 mW during 10 min. (d-f) Temperature change on the coverslip surface depending on the time and power of radiation for the corresponding wavelengths.

4. CONCLUSION

Temperature distribution along cell culture media was analysed using COMSOL Multiphysics. The simulation allows us to predict the optimal parameters of experimental singlet oxygen generation system excluding heating of cell cultures. It is important to note that some errors possibly occurred in the simulations generated by the input thermal and optical properties and the equations used.

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