Prevention, Treatment and Diagnosis of Pathogenic Infections by Using Pulsed Light Radiation Propagating Through Metamaterials

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Abstract. We propose novel optical methods for prevention, treatment and diagnosis of infections by pathogens using metamaterials with various geometries consisting of microspheres (i.e. photonic crystals, photonic molecules) and optical fibers structures. Around the adjacent elements of metamaterials appear the evanescent zones of propagated pulsed light radiation overlapping each other. This effect gives us the possibility to significantly increase the decontamination volume especially in non-transparent media. The parking geometries of microspheres and optical fibers ensure the efficient contact zone between the pulsed light radiation with contaminated materials (gases, liquids, tissues, implant surfaces). The penetration depth of evanescent field in contaminated materials can achieve values comparable with pathogens dimensions. We propose an attractive antimicrobial strategy using combined action of ultrashort pulses with different frequencies and pulse duration to achieve the selective decontamination of microorganisms with minimal effects on the components of human cells and tissues. We take into consideration the intrinsic symmetries of microorganisms protein structures (inclusive virus capsids) and their possible resonant excitation in double frequencies induced Raman scattering. The development of nonlinear models of the excitation of vibration modes of biomolecules of viruses and bacteria are revised taking into consideration the multi-mode aspects of interaction of pulsed light with excited biomolecules of pathogens. This method opens new possibilities in decontamination and diagnosis of the new collective processes, which can take place in viruses, bacteria, or other cellular structures under the action of external light pulses. Exponential distribution of radiation in evanescent zone gives us the possibility to capture and trap the viruses and bacteria along the optical fibers or/and microsphere surfaces.

1. Introduction
In this paper we take into consideration the symmetry of protein structures of pathogens (inclusively virus capsids), which plays an important role in the proposed vibrational method of pathogen-destroying mechanism [1-3]. In this case, for manipulation of viruses and bacteria, we considered the evanescent zone of metamaterials consisting of microspheres and optical fiber structures with various topologies [4-6]. It is demonstrated that using metamaterials such as photonic crystals it is possible to significantly increase the decontamination volume especially in non-transparent media. This volume can fill all free space between the fibers or microspheres, when the evanescent fields of adjacent fibers (or microspheres) are overlapping each other. The action of the field on viruses and bacteria must be estimated theoretically and experimentally demonstrated [7-8]. For the moment, there exists the
conceptual estimate model only. By developing such a technique one may be able to manipulate the microorganisms with the dimensions commensurable with the penetration depth of evanescent zone [9-12]. Taking into consideration that the depths of evanescent zone are not so large for short wavelength of radiation, one can be used long-wavelength radiation, for trapping viruses and bacteria near the surfaces of metamaterials elements so that the simultaneous actions of UVC and long-wavelength radiations effectively inactivate pathogens.

Most of all decontamination methods works on the UV lamps that emits nearly monochromatic light at 253.7 nm. Therefore, there is an increasing interest in pathogens decontamination not only for application in the industry but also for medical needs [14-15]. The bacterial contamination of any liquid or surface typically begins with the initial adhesion of only a few viruses that can then develop into a more structurally cohesive thin surface in a short time. Various methods with implication of UV radiation were elaborated for decontamination. For example, in the hospital, for decontamination of rooms and spaces are used germicidal UV lamps that work at 253.7 nm. This seems to be a good method for decontamination of viruses and micro-organism from air, however is not efficient. For large surfaces there are necessary high power sources, that are dangerous for patients. We show the possibility to use the evanescent zone created at the propagation of UV light through silica metamaterials, for disinfection of biological liquids.

The paper is organized as follows. A short description and characterization of the methods, experimental and theoretical approach. The setup and theoretical mechanism of the action of UV-radiation with viruses and bacteria are presented in section 2.

2. The Raman spectroscopy in the decontamination procedure

2.1. Objectives and methods of decontamination

Proposed efficient decontamination procedures using evanescent field of metamaterials opens up new perspectives and possibilities in inactivation of pathogens. The objectives of this paper are:

- To develop a method of decontamination using microspheres and optical fiber structures with various geometries.
- To demonstrate experimentally the efficient decontamination mechanisms which appear on the increasing of the contact surface of the evanescent zone in metamaterials.
- Different topological structures of meta-materials in order to increase the surface contact of pulsed light radiation with contaminated non-transparent media (implant surfaces, liquids (inclusively blood and plasma), gases)
- To find the new possibilities to trap and capture viruses, bacteria and other microorganisms from infected biological liquids along the fibers/microsphere surfaces, using the effective pulsed light radiation
- The possibilities to selective decontamination of pathogens without destroying the human cell components.

2.2. Characterization methods

As we known coherent anti-Stokes Raman spectroscopy (CARS) [1] reported an attractive tool for rapid vibrational spectroscopy. For dappling the Ultra short pulsed (USP) lasers in Coherent Raman Scattering (CRS) or CARS in the decontamination procedure of viruses and bacteria in many cases it is necessary to know not only in the relative dimensions of viruses and bacterias, but their symmetry too [2, 3] (see Figure 1). So far, general evolutionary pressures shaping capsid design have remained elusive, even though an understanding of such properties may help in rationally impeding the virus life cycle and designing efficient nano-assemblies.

The authors of Ref. [4] uncover an unprecedented and species-independent evolutionary pressure on virus capsids, based on the notion that the simplest capsid designs are the best, which was shown to be true for all available virus capsids. The theories result in a physically meaningful periodic table of virus capsids that uncovers strong and overarching evolutionary pressures, while also offering geometric
explanations to other capsid properties (rigidity, pleomorphic, auxiliary requirements, etc.) that were previously considered to be unrealatable properties of the individual virus.

Figure 1. Relative dimension of viruses (bacteria) and their commensurability with the evanescent zone of a fiber optics.

The UV radiation is largely absorbed by matter, and the purification of water or other biological liquid needs small volumes. In order to exclude this question, i.e., decontamination of small volumes, an efficient method was proposed, based on evanescent field technique created around silica metamaterials. When UV light is propagated through an optical fibre, significant quantity of radiation is spread outside of the fibre as an evanescent field that interacts with surrounding medium. Optical techniques play an important role for localization of nanometric and submicronic particles. Such methods, based on optical metamaterials (e.g., photonic crystals, optical fibres or cavities) where the penetration of evanescent field in the contaminated zone is primordial, can be used as an efficient decontamination procedure for viruses and microorganisms [13]. In the following, we provide a theoretical description of the interaction of UV radiation with viruses, explaining the physical mechanism. We present the experimental results that confirm the efficiency of decontamination method published in our previous paper [15].

3. Methods of decontamination

3.1. The connection between the methods of decontamination

Let's start from the traditional method of decontamination of liquids using UV-C pulsed light (see Figure 2 (LC1)). If we have a cylinder with contaminated liquid and this cylinder is irradiated from all directions with UV radiation, the total decontamination surface is $S = 2\pi R(L + R)$, where the first term indicates the lateral surface and last term represents the surface of the bases, $R$, represents the radius of the base, $L$ the length of the cylinder. So, if we use a classical method of decontamination, a big volume, of infected liquid remains contaminated $V_{cl} = \pi 2\pi R(L + R) dr$; $V_{con} = \pi R^2 L - V_{cl} \gg V_{cl}$ where $V_{cl}$ represent the efficient contamination volume, $d_r \sim \lambda$ is the penetration depth in liquid of UV radiation. Below we offer a method of decontamination using metamaterials for increasing of the decontamination volume. Sensing properties are expected to be related to nano-scale system dimensions. Let us firstly estimate the contact surface of flowing gas or liquid. In order to increase the contact surface of the contaminated liquid, below we proposed to examine the propagation of UV radiation through two types of meta-materials: type A corresponds to the packing of photonic-crystal fibers (PCF) and type B - photonic crystals (PC) (see Figures 2 (LC2) and (LC3) respectively), which both metamaterials are transparent for UV spectrum. If the PCF system is placed in a cylinder with contaminated liquid (see Figure 2 (LC1, LC2, LC3)), the liquid will fill all the space between the fibers.

The decontamination surface increases substantially $S_p = \pi r(r + 2rLN)$, where $N$ is the number of fibers from PCF, $r$ is the radius of one fiber. Last term represents the lateral surface of the fibers.
Here, it is considered that the UV radiation is inserted by fibers in the cylinder, see Figures 2 (Lc2). The penetration depth of UV radiation (evanescent field) depends on the relative refractive indexes of fibers and contaminated liquid. The intensity of evanescent field is expressed by \( I = I_0 \exp[-z / d] \), where \( I \) is the intensity of UV light of evanescent zone at distance \( z \) from fiber, \( d \) is characteristic exponential decay depth \( d \sim \lambda / n_2 \) where \( n_2 \) is refractive index of the liquid medium, \( \lambda \) is the wavelength of light radiation. Let's find the connection with classical method of decontamination. For this we need to express the decontamination area through the number of fibers. The estimations show that small radius of fiber \( r \) is proportional to \( r \sim R / \sqrt{N} \). It is easy to obtain the following expression for decontamination area of \( N \) cylindrical fibers \( S_d \sim 2\pi RL\sqrt{N} \). Here, we observe that the decontamination surface is proportional to the square root from the number of fibers. The decontamination volume of liquid in this case is proportional to the expression \( V_d \sim 2\pi RLd\sqrt{N} \). It is not difficult to observe, that the increasing of decontamination volume is proportional to \( \sqrt{N} \) where \( (V_d / V_{cl} \sim \sqrt{N}) \).

Figure 2. Methods of decontamination: (Lc1) traditional decontamination; (Lc2) decontamination using PCF in the hexagonal packed bundle; (Lc3) metamaterial like photon crystal.

Figure 3. The possibilities of the arrangement of quantum cavities.

But it is not clear what happens with other free volume between the fiber, which is situated at larger distance in comparison with \( \lambda / 2 \). This volume may be involved in the contamination zone, if
we continue to decrease the thickness of fiber. We may estimate the free volume between the fiber and the possibility to use all this volume with the decreasing of the fiber diameter. In the standard hexagonal packed bundle we may estimate the free volume between three fibers $V_f = r^2(\sqrt{3}-\pi/2)L = 0.18r^2L$. In this case the free volume in the big bundle doesn't depend on the fiber diameter and is equal to $V_f = \pi R^2 L(\sqrt{3}-\pi/2)$. The unused volume may be estimated $V_u = \pi RL(0.18R-\sqrt{N})$. When this expression achieved zero value all volume between the fiber can be used for decontamination of fluids. This corresponds to the following expression of fiber radius $r \sim R/\sqrt{N} \sim \lambda/0.18$. The similar expression can be obtained for other type of packing of the fibers.

Using the same method, we have estimated the decontamination surfaces of metamaterials $S_d = 4\pi r^2 N \sim \pi L^2 N^{1/3}$, (see Figure 2(Lc1, Lc2, Lc3)) like PC where $L$ is the edge length of the cube, $r$ is the radius of one micro-sphere, $N$ is the number of micro-spheres of the metamaterial. The liquid will fill all space between micro-spheres. The decontamination volume can be expressed in following form $V_d \sim dS_d = 4\pi dR^2 N^{1/3}$. In this estimation we can mention that increasing of decontamination volume depends on the number of microspheres, described by the dependence $N^{1/3}$. Although, at first glance it appears that the decontamination volume is lower than in PCF case, this is only an illusion. Due to the fact that number of micro-spheres in metamaterial like PC is much larger than the number of fibers in PCF, the decontamination volume in the second case is much higher. Another priority of last metamaterial consists in the fact that this works in all directions symmetrically, in comparison with PCF. The free volume between balls in a photonic crystal can be presented in the form $v_f = 8r^3(1-\pi/6) \sim 0.48V_f$. The free volume between the large cube with dimension $L$ have same proportion $V_f \sim dS_d = 4\pi dR^2 N^{1/3}$. In this case the difference between the $V_f - V_d$ is proportional to $V[0.1/3/(2L)]$. When the $L < \pi N^{1/3} / 0.98$, the increasing of surface becomes impossible and the classical aspects of evanescent zone is not acceptable. In this case, the volume between the balls may be regarded as a decontamination free volume. The wave is regarded as a quantum cavity for the standing wave (see Figure 3). The metamaterials, such as optical fibers or periodic photon structures open the novel possibilities to manipulate and kill viruses and bacteria in contaminated zones of liquids or organic tissue. For example, the good contact area between the implant and cells can be accomplished using such metamaterials on the surfaces. The guided UV radiation along the implant surface maintains the best medical assistance of contact surface against possible viruses or bacteria.

3.2. Experimental procedures and theory

The UV action against bacteria and viruses depends on the depth and volume of the evanescent zone of the periodical waveguide structures. In Figure 4, we represented such a periodical structure (fibers and spherical metamaterials), introduced into a cylinder through which the contaminated fluid flows. Taking into consideration the traditional conception of decontamination and possible decontamination volume in the evanescent zones of fibers or periodical bubble structures (see Figure 4), we may introduce the relative decontamination coefficient $\rho = V_d / V_f$. Considering that the lateral surface of the cylinder is larger than the surfaces of its two bases, we obtain the following expression for the relative decontamination volume $\rho \sim d\sqrt{N} / d_p$. The similar expression can be introduced for metamaterials like PC if we filled the cylinder with periodical bubbles of $SiO_2$. In this case the relative decontamination coefficient is $\rho \sim dN^{1/3} / d_p$. Here the classical decontamination volume is considered the penetration of the radiation into the spherical elementary volume $4\pi R^2 d_p$ with the width $\Delta R \sim d_p$. 


Figure 4. (Lc1) Reactor for UV decontamination. The UV radiation is generated by 6 UVC lamps and it is reflected in the center of decontamination region, where it is placed a cylinder, filled up by quartz microspheres. (Lc2) The cylinder filled up by quartz microspheres. (Lc3) Schematic representation of reactor for UV decontamination.

Figure 5. The preparation of mixed decontamination equipment, which use the UVC lamps and laser pulses. Lc1. On the bottom part of the figure is applied the canal for laser beam represented by black circle. Lc2. The final version of decontamination equipment in which laser pulses are sent through the black part of central core.

The combination of SiO, the PC with PCF improved the decontamination contact surface according to our preliminary investigations. The research of the efficient action of UV pulses on the chemical reactions, which take place in the microorganisms, is in the initial stage of our studies. Another effect which can appear in the process of decontamination is connected with the trapping of pathogen particles (viruses and bacteria) near the surface of fibers (or spheres). This effect is well known in the literature [5]. It consists in the attractive force acting on the particles with higher refractive indexes relative the refraction index of liquid index and appears due to the large gradient of EMF in the evanescent zone near the fiber Figure 5 (sphere Figure 4(Lc2)).

The system of quartz fibers with periodical structures irradiated simultaneously with 5 UV-C lamp and nanosecond laser pulses effectively decontaminates the bacteria and fungi (yeast) present in
translucent fluids. The process of development of this equipment which use both method of decontamination is presented in Figure 5. The last studies demonstrate that the UVC radiation becomes the effective method for inactivating bacteria, viruses, fungi and other micro-organisms. According to the literature [1-4] the special UVC radiation is an effective, environment-friendly and chemical-free method to dystrophy dangerous pathogens in any condition. On the other end, UVC doesn't pass the atmosphere, so it normally doesn't contribute to DNA damage, but it deserves to be mentioned that UVC lamps are used to kill bacteria and bedbugs. As a consequence, a local vibration energy of the modes may be coupled by an-harmonic non-linear term. For example, two vibration defects in cell replication and lead to cell death afterwards. The increasing of popularity of fiber system interaction with fabrics structures of clothing and the diversity of the optical schemes and methods of decontamination opens the opportunities for innovative research performing in this area. The scientific studies are stimulated also by a lot of incidence of short and long-term complications in the hazard situations, which took place decontamination of infected the fabrics (for example fabric clothing) used by people. One of them is when the fabric for cloth clothing adhesion with UVC is not in a good compatibility with decontamination sources (is not transparent or scatter the radiation so that the decontamination in the volume of material becomes impossible). Taking into consideration the metamaterials popularity, like PCF, it was decided to use these optical systems in their adhesion and penetration into a volume of fabrics killing the pathogens from fabrics and rooms inventory.

In our opinion, intrinsic topology of capsids may help to take into consideration more exactly the symmetry vibration modes of this virus structure, in order to estimate the possible anharmonic excitation of virus components by selectively distrusting them during the coherent Raman excitation.

Let us follow the excitation method of local vibration modes of biomolecules, like α or β tubulins for microtubules of dangerous bacteria [6] (see Figure 6) or capsids for viruses.

![Figure 6](image)

**Figure 6.** (Lc1) Comparison of the architectures of a 5-proto-filament bacterial micro-tubule A represents the B and A tubs in dark - blue; B tub is in light-blue and B: a 13-proto-filament eukaryotic micro-tubule: α-tubulin in white β-tubulin in black. Seams and start-helices are indicated in green and red, respectively C form indicates the biomolecular structure of α and β tubulines. (Lc2) The dependence of the potential energy of the non-linear oscillator on the two normalized modes $x = \sqrt{M/2\Omega Q}$, $y = \sqrt{M/2\Omega \Theta}$. (Lc3) Energy scheme for nonlinear potential with Raman excitation.

Taking into consideration that a local vibration energy of the prin structures of pathogens Figure 6 may be described by anharmonic nonlinear term. For example two vibration modes Q and Θ can be represented as a symmetric function relative to the square value of these normal coordinates.
Here $M_i$, $\Omega_i$ and $\kappa_i$ are the effective mass, frequency and anharmonic parameter for the vibration mode $i$ ($i=q, \theta$); $\kappa_{\theta,q}$ is nonlinear coupling of the normal modes of molecule oscillations. Anharmonic terms introduced in the Hamiltonian describe the possible destroying of this system by higher excitation. Let us consider two situations of the vibration of this molecular system represented by tubulins in protein packing in the microtubule of bacteria. We introduced collective nonlinear coupled modes like phonons in the condensed matter [7], described by above vibration model, for which two modes, $Q$ and $\Theta$ become aperiodic according to the theory of catastrophe [8], for higher excitation of the system by short laser pulses [2, 9] with the pulse duration, $\tau_L < 1/\Omega_j$.

\[
H_0 = \frac{M_q}{2} \left( \frac{dQ}{dt} \right)^2 + \frac{M_\theta}{2} \left( \frac{d\Theta}{dt} \right)^2 + \frac{M_q \Omega_q^2 Q^2}{2} + \frac{M_\theta \Omega_\theta^2 \Theta^2}{2} - \kappa_q Q^4 - \kappa_\theta \Theta^4 - \kappa_{\theta,q} \Theta^2 Q^2. \tag{1}
\]

Here we have introduced the attenuation constant, $\Gamma_j$, of each coupling modes through nonlinear interaction, $\chi_j = \kappa_j / M_j$. The anharmonic term of each modes is described by the nonlinear constant $\chi_j = k_j / M_j$. The an-harmonic potential is described by the two dimensional localization potential. The external, short laser pulses interact with the molecular dipole of virus components, so that in the simple representation, this has the traditional form $H_j = -(\mathbf{P}(E), \mathbf{E}(t,z))$. Following the traditional representation [10, 11] the laser field induce the polarization of biomolecule, the components of which in the similar representation has tensor character, which depends on the symmetry of excited molecules (virus's or bacteria's components) $P_j(E) = \alpha_j(E_j)$, where due to the tensor character of proposed two modes of oscillations, we decompose the recognizability $\alpha_j(Q, \Theta)$ in Taylor serial decomposition relative the normal components $Q$ and $\Theta$.

\[
\alpha_j \approx \alpha_j^0 + \frac{\partial \alpha_j}{\partial Q} Q + \frac{\partial \alpha_j}{\partial \Theta} \Theta + \varepsilon(Q^2; \Theta^2; Q\Theta) \tag{3}
\]

Introducing the expression (3) in interaction Hamiltonian we observe that the interaction with the local vibration modes can be described by the function $U_j = \alpha_j(E_j, Q_j)$, where $Q_j = Q_j$ and $\Theta_j = \Theta_j$ and the tensor $\alpha_{jk} = \frac{\partial \alpha_j}{\partial Q_k}$ must be maximally symmetrical according to the symmetry of the virus or bacteria biomolecules. Considering that laser pulse has same polarization, we represent it through the time dependent Gaussian function $E_j = E_0 \exp[-(t/\sqrt{2\tau_L})^2] \cos(\omega t)$. We substitute the generalized driving forces $F_j = -\partial U_j / \partial Q_j$ in the system of equation (2) and represent the solution in the linear approximation $Q_j = Q_{0j} \exp[-\Gamma_j t] \sin(\Omega_j t)$, where the amplitude has the following dependence on the intensity, $E_0^2$, pulse duration, $\tau_L$, and local osculation frequency $\Omega_j$ of the normal mode $j$ presented below.
\[ Q_{0j} = \frac{\sqrt{\pi \tau_j E_0^2 \alpha_j}}{2\Omega_j} \exp[-(\Omega_j \tau_j)^2 / 4]. \quad (4) \]

Observing the same exponential dependence on the \( \Omega_j \tau_j \), as in the Refs. [2, 9], we address the problem so as to excite the system of coupling oscillators, so that the "nonlinear frequency" Formula 5.

\[ \sqrt{\Omega^2_q - 4 \chi_q \langle Q^2 \rangle - 2 \chi_{q \phi} \langle \Theta^2 \rangle} \quad (5) \]

Achieved zero value, which corresponds to destroying of the local vibration mode after the finite number of short laser pulses. For doing this, let us consider the set of consecutive pulses "n", which are generated in the time interval \( T < \Gamma_j^{-1} \), so that the cumulated energy by the local oscillator after the predecessor pulses may be used in the next pulse excitations. For example, after first pulse the amplitudes of \( Q \) and \( \Theta \) models are described by the expression above expression. We obtain the following mean values of \( Q^2 \) and \( \Theta^2 \), Formula 6.

\[ \langle Q^2 \rangle = \left( \frac{\pi \tau_L^2 E_0^4 \alpha_j^2}{22 \Omega_j^2} \right) \exp[-(\bar{\Omega}_q \tau_j)^2 / 2] \quad (6) \]

Where \( \bar{\Omega}_q = \sqrt{\Omega^2_q - 4 \chi_q \langle Q^2 \rangle - 2 \chi_{q \phi} \langle \Theta^2 \rangle} \). This procedure of excitation of non-linear oscillator may continue till one of the amplitude of oscillation achieved the maximal separation line of nonlinear potential function \( U(Q, \Theta) \) as represented in Figure 5 (Lc2). It corresponds to the situation for which one of frequency achieves the zero value after "n" short pulses \( \Omega^2_q - 4 \chi_q \langle Q^2 \rangle - 2 \chi_{q \phi} \langle \Theta^2 \rangle = 0 \); or \( \Omega^2_{\theta} - 4 \chi_q \langle \Theta^2 \rangle - 2 \chi_{q \phi} \langle Q^2 \rangle = 0 \).

4. Conclusions

We propose new methods of decontamination with applications in medicine and public health. These methods contribute to an important increasing of the rate and volume of decontamination by increasing the contact zone between the light radiation and the contaminated environment (gases, liquids and solid surfaces). Regarding implants, a fine metamaterial coating on the implant surfaces not only contributes to the decontamination of the implant-tissue contact, but can also be beneficial for improving both of mechanical contact between the optic network of the metamaterial - patient's organic tissue and the processes taking place in immediate proximity to the irradiation area. A special attention will be paid to the propagation of short light pulses through such metamaterials. They will provide a selective interaction with the pathogen biomolecules having a negligible destructive action on human tissue components. The paper contains both an application and a fundamental aspect. Many of the effects of decontamination and capture of viruses and bacteria along metamaterial surfaces are seen, for example, in the transport of nutrients to the surface of tubules. So the development of metamaterial contact techniques with organic tissue opens up new possibilities for the prevention, monitoring and treatment of pathogenic diseases in different environments, including implantology. Here we can refer to different types of implants, such as implants for the heart, wrists implants, dental implants. Another field of application of the proposed decontamination methods directly addresses the issues of selective decontamination of the blood components. An important aspect of the fundamental part of the project is that we propose the development of the vibrational model of microorganism.
inactivation for a deeper understanding of the non-thermal selective action mechanisms on microorganisms taking into account both the duration, frequency and intensity of radiation pulses, as well as the basic characteristics of pathogens (dimensions, form, including capsid viruses, encapsulated or non-encapsulated viruses, internal symmetry of protein structures, types of bonds in biomolecules, single / double stranded nucleic acids, etc.).

5. References

[1]  Begley R F, Harvey A B and Byer R L 1974 *Appl. Phys. Lett.* 25 387-390
[2]  Yan J Y-X, Gamble Jr E B and Nelson K A 1985 *Chem. Phys.* 83(11) 5391-99
[3]  Blombergen N 1998 *Nonlinear Optics (4th Edition)* World Scientific
[4]  Mannige R V PLoS ONE 5(3) e9423
[5]  Kress H 2008 *Cuvillier Verlag* 140
[6]  Pilhofer M, Ladinsky M S, McDowall A W, Petroni G and Jensen G J 2011 *PLoS Biol* 9 e1001213
[7]  Zhu T and Ertekin E 2014 Phys. Rev. B 90 195209
[8]  Zhu T and Ertekin E 2015 Phys. Rev. B 91 205429
[9]  Gilmore R 1981 *Wiley-Interscience Publication* NY 1-2
[10]  Tsen S W D et al. 2012 *Journal of Biomedical Science* 19 62
[11]  Loudon R 2000 *The Quantum Theory of Light* Oxford University Press 448
[12]  Bazgan S, Ristoscu C, Negut I, Hapenciuc C, Turcan M, Ciobanu N, Mihaiescu I N and Enaki N 2015 *Rom. Rep. Phys.* 67(4) 1602–07
[13]  Enaki N, Bazgan S, Ciobanu N, Turcan M, Paslari T, Ristoscu C, Vascahsa A and Mihaiescu I N 2017 *Journal of Applied Surface Science* 417 40-47
[14]  Enaki N, Profir A, Bizgan S, Paslari T, Ristoscu C, Mihaiescu C, Badiceanu M and Mihaiescu I N 2018 *Metamaterials for Antimicrobial Biofilm Applications: Photonic Crystals of Microspheres and Optical Fibers for Decontamination of Liquids and Gases*, ch. 13. 27, *Handbook of Antimicrobial Coatings*, 1st Edition, Authors: Atul Tiwari, eBook ISBN: 9780128119839, Elsevier 596
[15]  Nahar Q, Fleibner F, Shuster J, Morawitz M, Halfpap C, Stefan M, Langbein U, Southam G and Mittler S 2014 *J. Biophotonics* 7(7) 542–551
[16]  Dai T, Vrahed M S, Murray C K and Hamblin M R 2012 *Expert Rev Anti Infect Ther* 10 185–195

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