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The use of hollow-core photonic crystal fibres as biological sensors

A.V. Malinin, Yu.S. Skibina, V.V. Tuchin, M.V. Chainikov, V.I. Beloglazov, I.Yu. Silokhin, A.A. Zanishevskaya, V.A. Dubrovskii, A.A. Dolmashkin

Abstract. **The results of development and study of a new type of a hollow-core photonic crystal fibre with radially increasing diameter of capillaries in the structured cladding are presented. The waveguide possesses a specific transmission spectrum and can be used as an efficient analyser of biological media.**

Keywords: *hollow-core photonic crystal fibre, transmission spectra, biological sensors.*

1. Introduction

Photonic crystal fibres (PCFs) [1–4] are, inherently, optical waveguides [5–8] differing from well-known classical silica optical fibres by a number of design features and the principle of light propagation. The cross section of a photonic crystal fibre reproduces the structure of a 2D photonic crystal [9–11]. In recent years the photonic crystals (dielectric media with spatial modulation of the dielectric constant) find applications in solving biomedical problems [12, 13].

Hollow-core PCFs may be manufactured using different methods. For example, the PCF structure can be formed by drilling regularly arranged holes in a quartz piece. In our studies we used the fibres made of borosilicate glass using the stack and draw technique [14]. Such glass has the refractive index 1.519 at a wavelength of 550 nm.

The optical properties of PCFs are not typical for optical waveguides. The transmission spectrum of a hollow-core PCF depends directly on the geometry of the structured cladding of the hollow core. Since the structured cladding is a 2D photonic crystal, photonic band gaps appear in the PCF transmission spectrum. The hollow core, in fact, is a crystal lattice defect, in which the guided modes are localised having no possibility to exit the waveguide structure.

The inner structure of a PCF is a medium with spatial modulation of the dielectric constant and, therefore, of the refractive index. Let the refractive index take only two values, n_1 and n_2, as the distance from the symmetry axis of the waveguide grows. Then, filling the channels of the waveguide with a liquid, we can vary one of the refractive index values. In principle, the variation in the refractive index should lead to essential change in the spectrum of reflection of light from the structured cladding and, therefore, in the spectral composition of the radiation, transmitted by the hollow core. The presence of absorbing or scattering molecules in the core is also expected to affect the radiation transmission. The possibility to get an optical response to the change in several medium parameters at once opens the prospect to use PCFs as sensor elements for complex analysis of biological liquids. Due to the design features of the waveguide, the analysis requires very small amounts of the material (tens of microlitres).

We designed and fabricated a new type of PCFs with the diameter of capillaries in the structured cladding growing from the symmetry axis of the waveguide to its periphery (Fig. 1). The transmission spectrum of the PCF with radially growing channels is always comb-shaped. The light propagation mechanism in such a waveguide consists in the reflection of radiation with different wavelengths from different layers of the inner waveguide structure [13, 15].

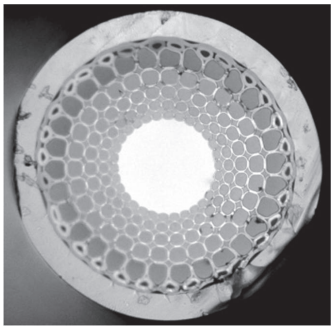

Figure 1. Cross section of a PCF with radially arranged capillaries. The outer diameter of the waveguide is 1013 μm, the diameter of the hollow core is 284 μm, the diameter of the channels in the first row is 26.92 μm, the capillary wall thickness is 2.28 μm.

The goal of this work is to reveal the optical response to the change in the optical properties of the medium, filling the channels of the PCF (absorption at definite wavelengths, refractive index and scattering). An important problem is to deter-

A.V. Malinin, Yu.S. Skibina N.G. Chernyshevsky National Research Saratov State University, ul. Astrakhanskaya 83, 410012 Saratov, Russia; LLC SPE 'Nanostructural Glass Technology', prosp. 50 let Oktyabrya 101, 410033 Saratov, Russia;
V.V. Tuchin N.G. Chernyshevsky National Research Saratov State University, ul. Astrakhanskaya 83, 410012 Saratov, Russia; Institute of Precision Mechanics and Control, Russian Academy of Sciences, ul. Rabochaya 24, 410028 Saratov, Russia; e-mail: tuchinvv@mail.ru;
M.V. Chainikov, V.I. Beloglazov, I.Yu. Silokhin LLC SPE "Nanostructural Glass Technology", prosp. 50 let Oktyabrya 101, 410033 Saratov, Russia;
A.A. Zanishevskaya N.G. Chernyshevsky National Research Saratov State University, ul. Astrakhanskaya 83, 410012 Saratov, Russia;
V.A. Dubrovskii, A.A. Dolmashkin V.I. Razumovsky Saratov State Medical University, ul. Bol'shaya Kazachya 112, 410710 Saratov, Russia

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mine the character of influence of each medium parameter on the waveguide spectral characteristics separately.

2. The influence of the medium refractive index on the PCF spectral characteristics

The spectral characteristics of PCF depend both on the geometry of its internal structure and on the variation in the refractive index of the medium that fills the channels of the waveguide (Fig. 2). All spectral characteristics of the waveguides, presented in this paper, were measured using the experimental setup, schematically shown in Fig. 3. A halogen white light lamp was used as a radiation source. A PCF sample was fixed on a three-axis movable platform. A microscope objective ($40^{\times}$) was used to focus the radiation into the hollow core of the waveguide. The spectral composition of the radiation at the sample output was measured using the Ocean Optics HR4000 spectrum analyser.

The influence of the medium refractive index on the spectral characteristics of the PCF was studied by analysing the transmission spectra of identical samples of waveguides with the diameter of the hollow core 266 μm and the length 50 mm, filled with the aqueous solution of glucose. The concentration of glucose in the solution, introduced into the hollow core of the waveguide, gradually increased from one sample to another. The choice of aqueous glucose solution as a test medium is caused by the possibility to prepare solutions having the refractive index in the interval 1.33–1.39 and by the absence of light absorption by glucose molecules in the visible part of the spectrum. Figure 4a presents two transmission spectra of identical PCF samples after filling the core with glucose solutions having different refractive indices.

The sensitivity of PCFs to the variation in the refractive index of the medium manifests itself in the shift of intensity maxima in the transmission spectrum of the waveguide in response to the change in the refractive index of the medium, filling the waveguide channels. This can be explained by considering the structured cladding of the PCF as a set of successively enclosed dielectric cylinders. Then from one layer to another the refractive index takes alternate values n_1 or n_2. Let n_1 be the refractive index of the medium, filling the hollow core of the waveguide and the channels of the structured cladding, and n_2 – the refractive index of the material of which the waveguide is made (in this case glass). The light entering the hollow core of the waveguide is incident on the layered structure at some angle θ and, due to the Bragg diffraction [16, 17], is reflected from it. The necessary condition for the reflection is

$$2dn_1 \sin\theta = m\lambda, \tag{1}$$

where d is the layer thickness, λ is the wavelength of the incident light, m is an integer. Therefore, the change in n_1 causes the change in the values of λ, satisfying the condition (1). If the refractive index of the medium, filling the channels of the structured cladding of PCF, increases, then the transmission spectrum of the cladding is transformed, causing the corresponding change in the spectral composition of radiation output from the waveguide.

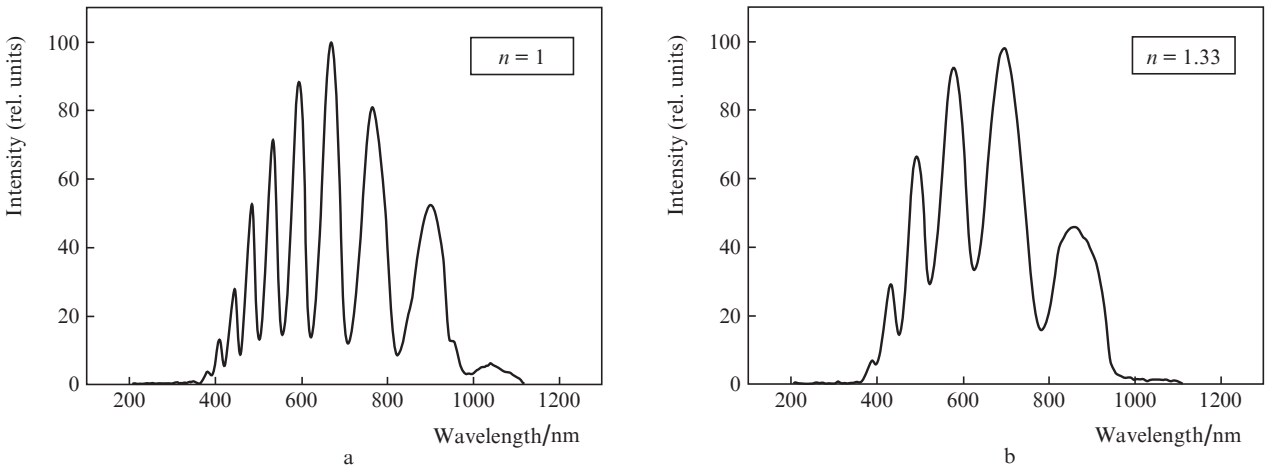

Figure 2. Transmission spectra of PCF samples with the outer diameter 720 μm and the diameter of the hollow core 266 μm. The waveguide channels are filled with air (a) and water (b).

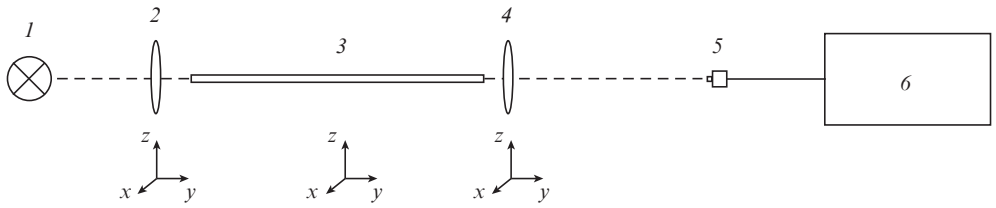

Figure 3. Schematic diagram of the experimental setup:
(*1*) radiation source; (*2*) microscope objective for radiation input; (*3*) PCF sample; (*4*) microscope objective for collecting the output radiation; (*5*) fibreoptic cable with collimator, connected with the spectrum analyser; (*6*) spectrum analyser. The elements (*2–4*) were mounted on movable platforms.

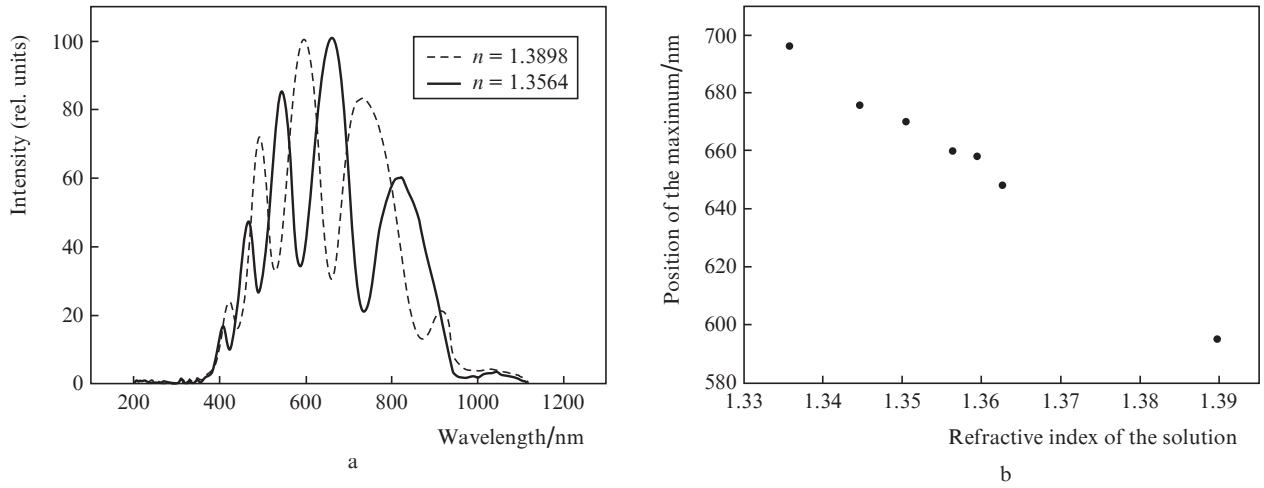

Figure 4. Transmission spectra of the PCF samples, filled with the glucose solutions with different refractive indices (a) and the shift of the local intensity maximum in the transmission spectrum of PCF with the growth of the refractive index (b).

3. Influence of the concentration of the optical radiation absorber on the spectral characteristics of PCF

Due to the presence of the hollow core, into which it is possible to introduce a solution, containing light-absorbing molecules, and in which the guided light modes are localised, PCFs may be used as an instrument for photometric analysis. Practically, spectrophotometric analysis of solutions is usually carried out using standard quartz cuvettes having the thickness up to 10–50 mm, which requires considerable amounts of the substance to be studied. Using PCF as an extensive cuvette one can perform analogous investigation probing a layer of absorbing medium as thick as a few centimetres or even a few tens of centimetres, the total amount of the substance being very small. Thus, to fill the PCF with the hollow core of large diameter (250 μm) and 50 mm long the volume of ~10 μL is required (for comparison, the volume of a standard quartz cuvette is ~3.5 mL). The increase in the thickness of the absorbing layer leads to greater attenuation of the probing light beam, which allows the analysis of solutions with low absorption coefficient and low concentration. Hollow-core PCFs may also find application in spectrophotometric analysis using luminescent probes.

The attenuation of the intensity of optical radiation in a collimated beam, passing through a layer of absorbing medium, is described with the Buger–Lambert–Beer law:

$$I(l) = I_0 \exp(-\varepsilon c L), \qquad (2)$$

where I_0 is the intensity of incident light; L is the thickness of the substance layer; ε is the molar absorption coefficient; c is the absorber concentration.

Aimed at estimation and comparison of the efficiency of the photometric method of analysis of solutions, the transmission spectra were measured for the aqueous solution of cyanocobalamin filling the 10-mm-thick quartz cuvette and the 50-mm-long PCF. The aqueous solution of cyanocobalamin strongly absorbs radiation in the visible wavelength region. One of the absorption maxima of the solution falls on 550 nm. The molar absorption coefficient at this wavelength is 12700 L mol^{-1} cm^{-1}. In the experiment the solutions with the concentration 0.001, 0.003, 0.005, and 0.007 mg mL^{-1} were used.

Figure 5a shows the spectrum of the optical radiation, passed through the quartz cuvette with the cyanocobalamin aqueous solution. The spectrum is normalised to the transmission spectrum of the cuvette with pure solvent. Figure 5b

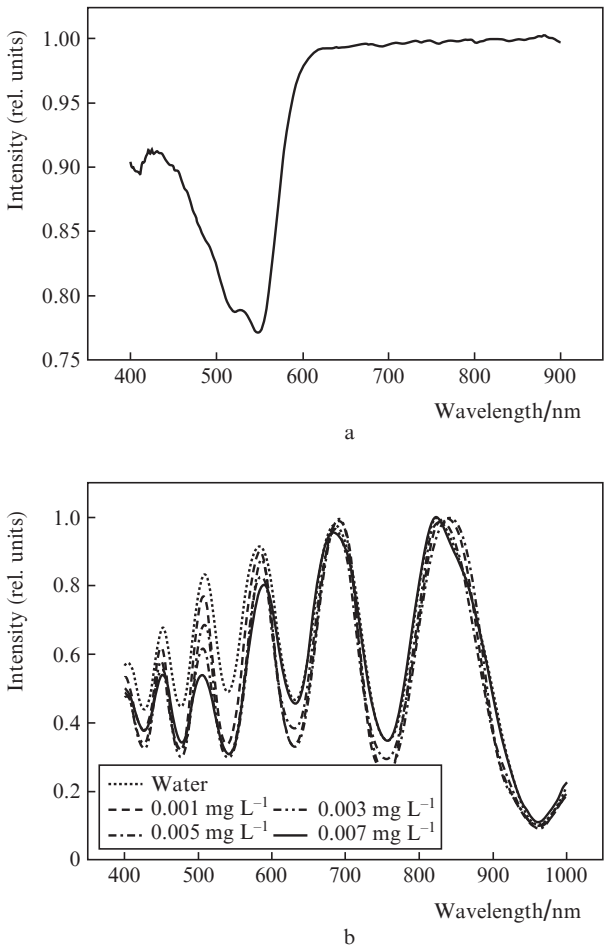

Figure 5. Transmission spectra of the standard quartz cuvette (a) and identical samples of PCF (b), filled with aqueous solutions of cyanocobalamin.

shows the transmission spectra of PCF samples with the hollow-core 284 μm in diameter and channels filled with the cyanocobalamin solutions with different concentrations. When increasing the concentration, in the transmission spectrum of the waveguide one can observe the lowering of the intensity maximum that overlaps the absorption band of the solution. The obtained heights of the maxima were normalised to the maximal transmission of the waveguide with its channels filled with pure solvent. Figure 6 presents the dependence of the normalised intensity at 507 nm, obtained in the experiment, on the concentration of the solution.

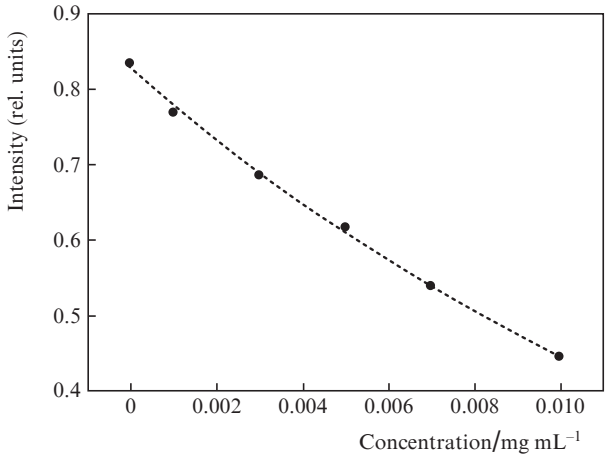

Figure 6. Dependence of the intensity of the optical radiation at 507 nm upon the concentration of the cyanocobalamin solution.

4. Influence of scattering on the propagation of radiation through PCFs

The optical properties (refractive index, absorption coefficient) of the medium, filling the hollow core of the PCF, exert significant influence on the spectral characteristics of the waveguide. The growth of the medium refractive index leads to the displacement of the transmission bands, the absorption causes attenuation of radiation in the core within definite spectral regions. The effect of scattering manifests itself in degradation of transmission performance in the whole visible region of wavelengths. The introduction of scattering particles into the hollow core leads to attenuation of the radiation passed through the waveguide. The photons that have changed the direction of propagation after the scattering event either propagate along the core back to the source of radiation, or leave the core and enter the cladding, because the angle between the propagation direction and the surface of the cladding no more satisfies the Bragg reflection condition.

Detecting the change of the PCF transmission caused by the increase in the concentration of scattering particles in the hollow core of the waveguide provides the basis for the method of blood grouping in humans.

The human blood is an opaque turbid medium, comprising 55 vol.% of plasma and 45 vol.% of cells. The blood comprises multiple cell types that affect the scattering of light. Nearly 99% of cells are red blood cells (erythrocytes) – acaryocytes having the shape of a biconcave disc 5.7–9.3 μm in diameter [18] and 1.7–2.4 μm thick [19].

The human red blood cells contain multiple group antigens, forming the group systems, among which the ABO system is of primary importance for medical practice. This group system comprises two erythrocyte antigens, denoted as A and B, and two types of plasma antibodies, anti-A (a) and anti-B (b). The blood of a human cannot contain antigen A and antibodies (a) (or antigen B and antibodies b) simultaneously, because the interaction of these nonspecific proteins would cause cell–cell adhesion of erythrocytes (the agglutination reaction). The presence of definite agglutinogens (antigens) and agglutinins (antibodies) in the donor and recipient blood determine the hemotransfusion compatibility.

In the course of the agglutination reaction the erythrocyte complexes arise in the blood containing from a few units to a few tens of red blood cells. In the classical method of blood grouping the formation or the absence of such complexes after adding specific agglutinating serums to the whole blood is a signature of the blood belonging to a definite group. However, the agglutination reaction is not always clearly marked because of low activity of the used agglutinating serum or occurs after a long period of time. Although the error percent in classical blood grouping is minimal, it is of interest to develop an automated method, allowing fast response to even weak agglutination reaction and, what is also important, to provide significant reduction of the trial blood volume and the agglutinating serum consumption.

The optical properties of blood (including the light scattering) are mainly determined by the presence of red blood cells. One of the approaches to the description of scattering in the blood is the radiation transport theory [12, 20], in which the parameters used are the absorption coefficient μ_a, the scattering coefficient μ_s, and the anisotropy factor g (the mean cosine of the scattering angle for the elementary volume of the medium). These parameters are determined by the size of red blood cells, real and imaginary parts of the complex refractive index ($n + i\chi$) of red blood cells (Fig. 7) and blood plasma [18]. According to [21], the scattering coefficient is expressed as

$$\mu_s = (1 - H)\sum_{i=0}^{M} N_i \sigma_{si}, \qquad (3)$$

where H is the hematocrit; M is the number of volume fractions of red blood cells; N_i is the number of particles having the ith diameter in the unit volume of the medium; σ_{si} is the scattering cross-section of the particles of the ith diameter.

When the agglutination reaction of red blood cells is positive, a large number of produced erythrocyte complexes sub-

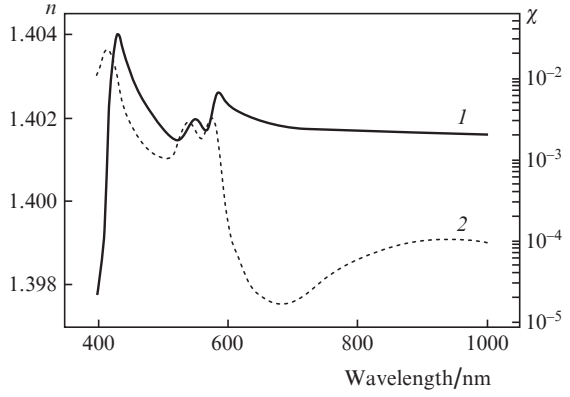

Figure 7. Dependences of the real (*1*) and imaginary (*2*) parts of the refractive index of red blood cells upon the wavelength [13].

side at the bottom of the agglutination tube. As a consequence, the number of erythrocytes suspended in the solution is reduced, which, in accordance with (3), results in the reduction of the medium scattering coefficient.

In the experiment the mixture, consisting of blood diluted with saline and agglutinating serum, was introduced into the hollow core of the PCF sample. The waveguide sample was subject to irradiation from a broad-band source, and the output radiation intensity was measured in the wavelength region 400–700 nm. The dilution of whole blood with saline up to hematocrit less than 1% was undertaken mainly for getting the output values of the radiation intensity, sufficient for the analysis. The first solution was prepared by adding the agglutinating serum from the A group to the test tube with whole blood belonging to the B group (positive agglutination reaction) followed by dilution with saline up to the 0.8% hematocrit after ten minutes of incubation. The second solution was prepared following the same algorithm, but using the agglutinating serum B (negative agglutination reaction in the test tube).

Figure 8 represents the averaged transmission spectra of identical PCF samples with the 270-μm diameter of the hollow core, filled with the prepared solutions. From the figure it is seen that the maximal radiation intensity at the output from the sample (λ = 662 nm) in the case of positive agglutination reaction reaches 55 units, while in the case of negative reaction it is only 29 units, so that the ratio of the output intensities for different reactions I_+/I_- is equal to 1.9. The spectra presented in Fig. 8 are the result of averaging over five measured spectra a transmission for identical samples of 50-mm-long waveguides for each solution. All obtained intensity values are summarised in Table 1.

For the differentiation of reactions one can use the rule of three standard deviations and introduce the interval δ, defined by the inequality

$$\langle Y\rangle - 3S_n \leqslant \delta \leqslant \langle Y\rangle + 3S_n. \quad (4)$$

According to (4), for the wavelength λ = 662 nm the agglutination reaction should be considered positive if the measured value of the optical radiation intensity at this wavelength falls within the interval from 51.62 to 58.57, and negative within the interval from 26.61 to 33.29.

Table 1. Estimate of the measurement error of the intensity of optical radiation (λ = 662 nm) emerging from the PCF samples filled with the solutions of the products of blood reactions and standard serums (produced by protocol I).

Agglutination reaction +/– (Sample No.)	Y_i	$\langle Y\rangle$	$(Y_i-\langle Y\rangle)^2$	S_n	Δ	ε (%)
Reaction + (1)	55.687		0.406			
Reaction + (2)	50.845		17.682			
Reaction + (3)	55.037	55.05	1.502	1.142	4.878	8.86
Reaction + (4)	57.067		4.071			
Reaction + (5)	56.612		2.441			
Reaction – (1)	29.221		0.531			
Reaction – (2)	31.112		1.351			
Reaction – (3)	31.043	29.952	1.195	1.113	4.555	15.21
Reaction – (4)	32.396		5.986			
Reaction – (5)	25.987		15.704			

Note. Y_i is the coordinate of the local maximum of the radiation intensity at 662 nm found from the experimental data (i is the number of the measurement); $\langle Y\rangle$ is the mean arithmetic value of Y_i; S_n is the root-mean-square error in the results of a set of measurements; Δ are the boundaries of the confidence interval (error in the measurement results); ε is the relative error in the measurement results.

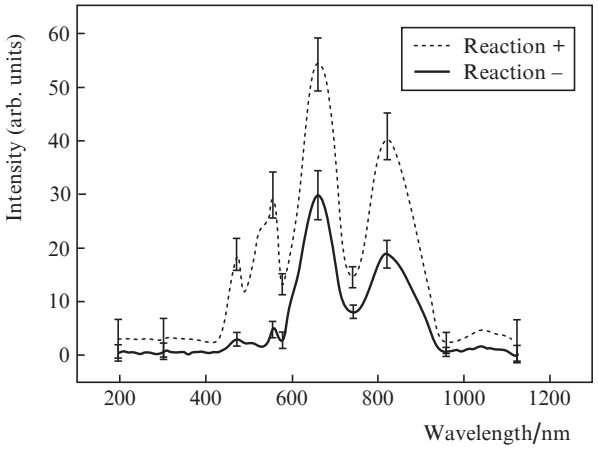

Figure 8. Averaged transmission spectra of identical PCF samples with the diameter of the hollow core 270 μm, filled with the products of positive (+) and negative (–) reaction of erythrocyte agglutination.

5. Conclusions

The data on the influence of the optical properties of liquid media (solutions, biological liquids), filling the internal structure of hollow-core PCFs, on the spectral characteristics of the waveguides are obtained. It is found experimentally that the increase in the refractive index of the medium leads to the shift of the transmission spectral regions in PCF samples. The presence of even small amounts of absorbing substance in the hollow core of the PCF causes strong radiation attenuation in the spectral range, corresponding to the absorption region. The radiation scattering in the medium, filling the hollow core of PCF, results in damping of the optical signal in the waveguide for all wavelengths. The dependence of damping on the radiation wavelength and the size of scattering particles requires an additional study.

Based on the obtained experimental data, we can announce the possibility to use PCFs as sensitive probes (sensors), particularly, in systems for automated blood groping in humans. The implementation of automated technique of blood grouping requires multiple additional research, using the blood samples from different donors. However, it is already clear that the simply implementable technology of fabricating hollow-core PCFs with a given internal structure may in future help to solve the problem of simple and reliable automated blood grouping.

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