The theoretical analysis of optical properties of blood

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Knowledge of optical properties of blood is very important to solve problems presented by biomedical optics. The development of predictive models of blood is a challenging task due to the inherent complexity of biological systems. In this paper, we investigated the optical parameter responsible for the appearance attributes of whole blood. Blood, an extraordinary fluid, makes life possible. The circulation of blood through the body results to function and fights diseases or infections. This work focuses on generative computational simulations, modelling, and deep learning techniques to gain data-driven insights about the valuable fluid of whole blood and its properties. The analysis of optical properties of blood is essential to interpret its interaction with light to accurately diagnose illnesses. In recent years, the studies of the association between blood and previously known symptoms have attracted increasing attention. The bibliometric analysis showed the trends of whole blood and its parameters in an increasing pattern. In this study, we proposed an interpretable deep learning strategy incorporating the neural network to examine the refractive index of blood data. The new proposed method fully employed raw data and allowed for implementation of a build-up and a validation model. The developed model was used to successfully diagnose, detect and define the diseases in a manner that is noninvasive, simple, accurate and completely cost-effective. These intelligent models can play an important role in future biomedical applications in design and improvements to be made on the performance of optical devices.

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1. Introduction

Nowadays, the method of examining blood parameters are attuned to reach ultimate sensitivity for diagnostic purposes in goal to more effectively fight disease and save valuable lives. Blood is an unmistakably important fluid for the body. The novel research focuses on the detailed investigation of a single species of blood for diagnostic purposes [1, 2]. The simple and rapid analyses of the blood that exhibits prolonged circulation in the human body could be used in diagnosis and evaluation of many diseases. Blood is composed of plasma, erythrocytes , leukocytes and thrombocytes are suspended in the plasma with other particulate matter [3]. The refractive index of blood depends on the concentration and distribution of these intracellular elements. Furthermore, refractive index depends on temperature. The refractive index as a function of wavelength determines its spectral variant of tissue interstitial fluid that in its turn defines the wavelength dependence of scattering properties of tissues [4]. The concentration of substances in the blood used has been anticoagulated to keep all the contents in suspension. The functions of blood in our body were transportation, regulation and protection. Firstly, the blood transports oxygen and hormones, provides nutrients, and removes waste products from cells. Secondly, the blood helps to keep the right body temperature, maintaining stable levels by adjusting blood vessels and the amount of heat. The blood temperature in the body is one degree higher than body temperature depending on the gender and location measured. At last, the platelets and solid parts dissolved in the blood plasma substance are used to protect wounds from infection and halt bleeding. White blood cells and certain chemical messengers also play an important role in the immune system. The widespread use of diagnostic methods of blood will provide great convenience in preventing and treating diseases. The researchers are investigating the blood data analyses with deep learning methods to diagnose diseases beforehand, in order to increase both life expectancy and quality. Deep learning has an exponential and leading role in solutions to existing predicaments. Another field where deep learning can be applied is development of diagnosis techniques, especially those that are based on processing experimental data for decision procedures. It is based on different algorithms and theories, exhibiting the characteristics of approximation and features of dispositionality. The advantages of this method serve as a proper solution for a cost-effective, tractable, high machine intelligence expressly quotient and less time-consuming than the traditional methods. The techniques with integrity provided by digital data assists the medical intelligent decision system. The information gathered is combined with high technology processes to provide analysis and interpretations of blood data. The examination and understanding of refractive index, $n_{refractive}\ (T,\ C, l)$, provide several advantages over diagnostic methods in use today. By the computational method, the light scattering properties, trends and the differences of blood parameters were effectively predicted and used in successful medical studies. Different diseases change the refractive index and makes it a candidate for biomarker. Precise knowledge of the dependence of concentration, temperature and wavelength are required for analysis the interaction of light with whole blood for purposes of clinical diagnostics [5, 6](?). The refractive index can determine the concentration of a solute in a solvent and be used as a temperature indicator due to its temperature dependence in fluids. The determination of refractive index has been carried out by using concentration and temperature of homogeneous solutions. The determination of optical properties of this valuable solution possesses intrinsic complexity compared to the basic measurements of a single microscopic cell. Blood isolated from the human body or the artificial blood used in measurement regardless, it is essential that the blood's temperature is carefully adjusted. Efficient and unerring blood temperature management is necessary to conduct and contain secure measurement mechanisms. Another factor in measurements is the dependence on concentration of haemoglobin obtained from red blood cells by breaking the cell membranes. The direct relation to both real and imaginary part of the refractive index [7-9]. For people in good physical conditions, the total haemoglobin concentration in their whole blood varies between 130 gL^{-1} and 160 gL^{-1}. The solutions with different concentrations in the visible and infrared wavelength range have been widely used in simulation and analysis of light scattering and microscopic data [10]. The researchers have comprehensively used these values in application-oriented investigations for biomedical applications. An important trend for the future of health technology will be the increasing use of artificial intelligence in-lieu-of traditional medical applications on grounds of increased competency and effectiveness. The fact that the intelligence of healthcare in the future must come both from artificial and conventional forms [11]. Newer and better medical technologies are being developed by using these frameworks. The application of artificial intelligence in healthcare has the potential to lower costs, broaden accessibility, expedite prognosis and can be a prime asset for patients and providers.

2. Motivation

The research on biological samples has tremendous improvements during the last decades. The motivation behind this research is based on the need for high-quality medical diagnostic methods. The main part of the clinical decisions is the diagnostic testing into modern healthcare systems [1]. Getting artificial intelligence into widespread real-world usage requires careful outlines of many important issues to be drawn. The study of blood parameters has been engineered for biomedical systems to manage novel functions and expand current biomedical applications for diagnostics. Extensive research has been done to map blood research and illustrate key research trends by running bibliometric research. This navigation on literature provided a promising avenue for our research. The well-known database of Web of Science (Clarivate Analytics (WOS)) and Scopus (Elsevier) were inspected for documents containing the word "blood". The WOS is a multiple database indexing service, and the Scopus is the abstract and citation database of peer-reviewed all scientific study areas [12, 13]. In these two databases, there was a quite high and rapid increase trend in the number of scientific articles for both blood and its parameters and illuminated that this research subject is novel and up to date. These articles were analysed and evaluated as "topics" in terms of all years, field parameters were also included. There are 1948992 (~1.95 million) and 3211060 (~3.21 million) articles on these two databases in their entire operating periods, respectively. In Fig. 1, it is seen that the trend and number of articles in WOS and Scopus contains both "blood" assigned to the right y-axis and "blood refractive index" to the left y-axis.

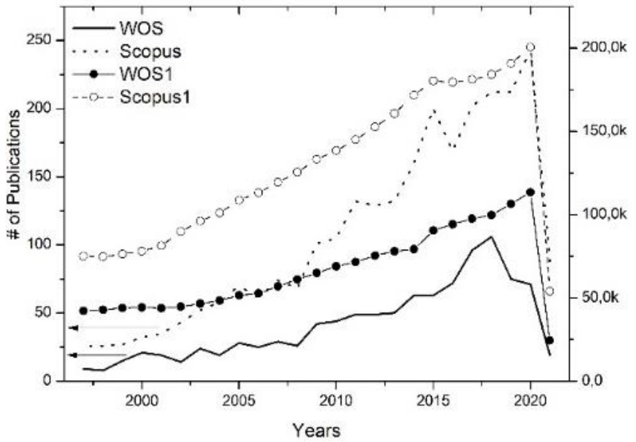

Fig. 1. Distribution of Number of Publications in WOS and SCOPUS database based on year

The patterns of published articles were different depending on the area of research interests. In WOS databases, the categories of blood topic searches are distributed as haematology (7.07%), pharmacology (6,58%), immunology (5.95%), medicine research experimental (4,36%), cell biology (3.15%) and engineering biomedical (2.16%) of the 1.95 million articles. The publication feature has been characterized by visibility and networking with many foreign research structures. The number of publications are currently increasing, so are the citations. This data is useful in cumulative and changing scientific knowledge and can aid in planning new studies for researchers. The total number of publications based on refractive index of blood were 1062, 68% of it being articles and 21% of it being proceedings papers in WOS between 2002 and 2021. The total number of citations to these articles tallies up to 15504 times and average citations per article were 21.33 in SCI/SCI-E index journals. There are 2657 articles in the Scopus database. The disadvantages of these databases are higher rate of duplicated citations, self-citation records and certain lack of standardization procedures [14].

3. Materials and methods

Understanding blood-light interactions for adaptive functions with concentration and temperature at different wavelengths can increase the awareness of fundamental facts of our body. The small changes in refractive index of blood as easily accessible biomarkers were calculated using the experimental data for medical applications to detect disease presence or even predict disease. Theoretical simulations of the refractive index of blood are difficult at different conditions. The refractive index includes two parts as

$$n = n_{\mathrm{Re}al} + in_{Imaginary} \tag{1}$$

where the n_{real} is the real and $n_{imaginary}$ is the imaginary part of refractive index, respectively. The real part represents the change in the speed of propagated light through a medium, compared to the speed of light in a vacuum. In this study, the experimental data for the refractive index of blood are collected form literature given in references [4, 5, 15-19]. The core of deep learning behaviours as a simulation method to predict parameters is the design of the artificial neural network (ANN) and may pave the way to new sophisticated systems. Recently, intelligent algorithms with optimized algorithms show a high potential in different medical fields. The ANN is based on the simulation of the neural network of the human brain. Some of the neurons activate the messages received from somewhere else and then pass them onto other neurons [20]. The learning methods are representation methods, obtained by composing simple but non-linear modules that each transform the representation at one lower level into a representation at a higher and slightly more abstract level [20]. The certain amount of training data is required for neural network algorithm. The neural network includes artificial neurons with three main components such as weight, bias, and transfer functions. The input parameters were temperature (°C), concentration (g/L), and wavelength (nm). The network was designed by using the attributes of neighbourhoods to train the network to produce the correct target data.

4. Results and discussion

The functions and the backpropagation algorithm were used to update the value of the connection strength parameter, weight, and bias parameters of each neuron in the neural network, therefore ending the process of training.

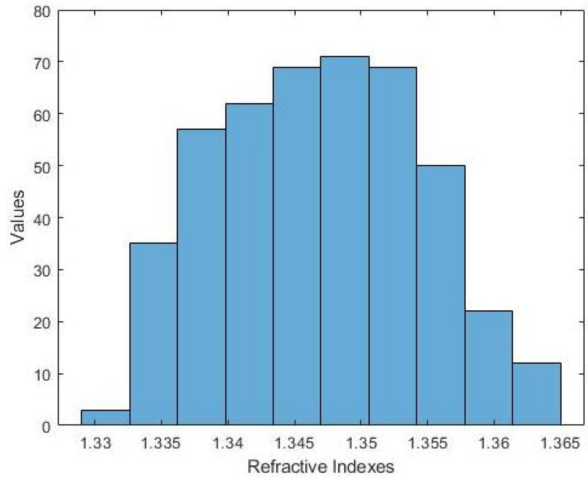

Fig. 2. Distribution of input data (color online)

Each input is multiplied by the corresponding weight parameters of the neuron connection. Next, a bias value is added to the summation of inputs according to the following equation

$$n_i = \sum_{i=1} w_i x_i + b_i \tag{2}$$

where w is the weight and b is the bias parameter. The summation (n_i) is converted as output with an activation (transfer) function. After feeding off training data, it is expected to be updated to a value more suitable for dealing with similar results. After the training process, the underfitting and overfitting results can be detected by using the test data. The learning curve during the testing process is checked by drawing, calculating the variance and the bias. The trained artificial neural network is used to predict the refractive index by backpropagation learning algorithm with the Levenberg-Marquardt (Trainlm) method. The trained network was used to determine refractive index and diseases with high efficiency. A literature survey has been performed for collecting the experimental data. The training and testing data were randomly selected among experimental results.

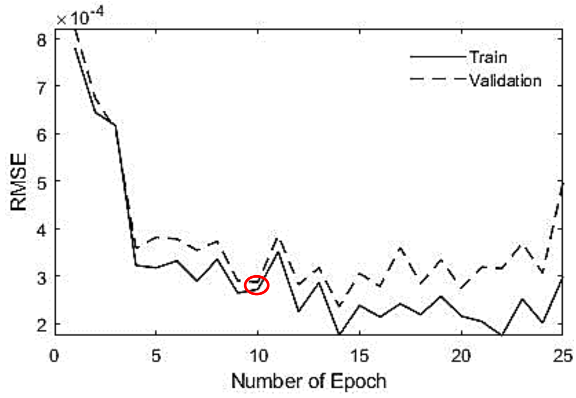

Fig. 3. RMSE of train and validation data to obtain optimum layer of neurons for hidden layers for refractive index model (color online)

The model and employed parameters affect the performance of the network. The duty in this network is the examination of the numbers of layers and neurons in the hidden layers to develop a model. For the optimal parameters and network, the trial-and-error approach was used to determine the number of neurons. The performance of the developed model was statistically evaluated with a specific criterion. The criteria consists of the correlation coefficient (R), while mean absolute error (MAE) and mean square error (MSE) were used as error evaluation.

Table 1. The statistical parameters of data

Training/Validation	R^2	MAE	MSE	RMSE
60/40	0,949	0,034	0,002	0,047
70/30	**0,968**	**0,030**	**0,002**	**0,039**
80/20	0,950	0,036	0,002	0,043

The correlation of coefficients of data given in Table 1 are sustainable for the performance of the network model. The MAE and MSE values of volume loss for training and testing sets are also acceptable. If the MSE reaches zero, the performance of the model is regarded as being excellent [21]. The prediction of the proposed model is in good agreement with the experimental data and all the errors are within justifiable ranges.

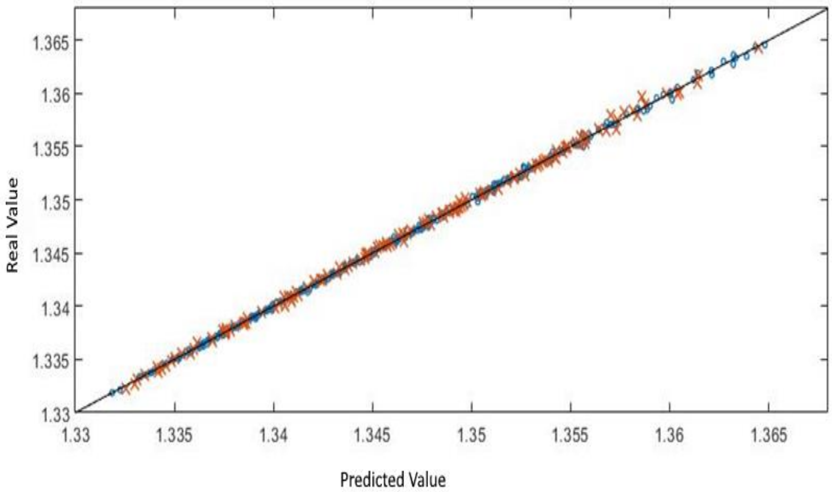

Fig. 4. Comparison of experimental or real (y-axis) and predicted (x-axis) values of refractive index

5. Conclusion

This study presented the development of a model to predict the refractive index of blood samples as a function of temperature, concentrations, and wavelength in the range of 20-45 °C, 0-200 g/L HbC and 436 to 1550 nm, respectively. The interaction and distributions of incident light at these conditions provide necessary information about the medical state of an individual. The behaviour of the refractive index of blood was expanding by the proposed model. In this study, a novel model for the predictive simulation of refractive index of blood with constituents was investigated. This model shows a close quantitative and qualitative agreement with actual measured data and experimental observations reported in biomedical literature. In the accuracy of the trained neural model, all values are bigger than 0.95 and the predicted model aces a high reliability rate. The low mean absolute error for predicted values shows that the model is quantitatively and qualitatively admissible. Hence, it was concluded that the proposed model is a successful and advantageous tool for determining the optical parameters of blood with considerable savings in cost and time. The advantages of this study should indicate the scope of diagnostic tests available for use at the point-of-care and in turn contribute to the potential, capability and accessibility of rapidly developing area of medical diagnostic technologies.

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