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Shaped beam scattering from a single lymphocyte cell by generalized Lorenz–Mie theory

Jia Jie Wang [a,*], Lu Han [a], Yi Ping Han [a], Gerard Gouesbet [b], Xuecheng Wu [c], Yingchun Wu [c]

[a] School of Science, Xidian University, Xi'an 710071, China
[b] Laboratoire d'Electromagnétisme des Systèmes Particulaires (LESP), UMR 6614 du CNRS, BP12, avenue de l'université, technôple du Madrillet, 76801 Saint-Etienne-du Rouvray, France
[c] State Key Laboratory of Clean Energy Utilization, Zhejiang University, Hangzhou 310027, China

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ABSTRACT

With the aim of improving the measurement capabilities of laser-based diagnostic instruments for cells, an eccentric stratified dielectric sphere model illuminated by an arbitrary shaped beam is applied to the modeling of light scattering by a single nucleated cell within the framework of the generalized Lorenz–Mie theory (GLMT). A particular attention is paid to the study of scattering properties of a lymphocyte cell from an arbitrary incident Gaussian beam. Numerical results concerning the influence of shaped beam parameters (beam waist radius, incident angle, location of beam center) as well as of cellular parameters (ratio of nucleus size to cell size, location of the nucleus within the cell) on the scattering properties are presented and discussed, with comparisons to the scattering behaviors from a concentric stratified sphere model. The results reveal that the forward scattering intensities are mainly determined by the cell size regardless of the nucleus/cell ratio, while sideward scattering signals are sensitive to the change of cell internal structure. As the beam waist radius varies, the scattering patterns in the present cases are similar to each other, although the absolute intensities are different. Additionally, location of the nucleus within the cell, incident angle of the beam as well as location of the beam waist center play significant effects on the light scattering intensity distributions.

1. Introduction

The human white blood cells (WBCs), which are also known as leukocytes, are very important components in human blood due to their significant role in controlling various disease conditions and eliminating invading microorganisms. Five types of WBCs are normally found in human blood: two types of mononuclear (lymphocytes and monocytes) and three types of granulocytes (eosinophils, basophils, and neutrophils).

In normal conditions, lymphocytes occupy around 20–44% relative to all WBCs population. These cells play a highly important role in the human immunity against microorganisms and other sources of foreign macromolecules. Specifically, the T-lymphocytes constitute a large part of the human lymphocyte population, they act against virus infected cells and tumor cells, while the B-lymphocytes confer immunity through the production of specific, soluble antibodies. Their quantitative levels and morphological distribution are regarded as the most important indicators among others in clinical diagnosis and immunity research [1].

In recent years there has been an increasing interest in light scattering by lymphocytes due to the fact that light

* Corresponding author. Tel.: +86 02988200182.
E-mail address: wangjiajie@xidian.edu.cn (J.J. Wang).

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scattering is able to provide an exquisitely sensitive approach for real-time, non-intrusive and sometimes label-free determination of cellular shape as well as internal structure, consequently leading to accurate cell identification and sorting. A prominent example of applications is the development of flow cytometry for cell discrimination based on light scattering signals [1–3].

With decades of improvement, advanced instruments, such as the scanning flow cytometry (SFC), are now able to perform the measurement of light scattering patterns of cells [2]. To obtain the cellular features based on the measured light scattering patterns, researchers normally turn to the comparison of experimental data with simulated results since there is no general solution for the inverse scattering problem. Thus, fulfilling the potential of light scattering techniques for cell diagnosis requires a continuous development of accurate as well as efficient characterization methods, the primary task being to develop a proper optical model for the scattering problem under study, and then to solve corresponding direct and inverse light scattering problems.

Concerning the optical model, the better we know the morphological features of cells and the description of the incident light, the more reliable solutions could be obtained and the more the problem of cell characterization is accurately solved. Generally, fundamental ingredients, including optical parameters and morphometric features, are needed to build a precise physical model for cells. On one hand, the optical parameters of cell constituent are still an open question since they are not available in a reliable, complete form, as we will discuss later in Section 3.1. On the other hand, the morphometric features of the cell are rather complex. It might take into consideration, for example, some nonsphericity of the cell and its nucleus, quantitative data on an eccentric nucleus location within the cell, cell surface texture, and so on.

Depending on the complexity of the cell structure, several optical models were proposed to the simulation of light scattering by cells along with the development of light scattering theories, including analytical methods, e.g. generalized Lorenz–Mie theory [4], various numerical methods, e.g. finite difference time domain method (FDTD) [5], discrete dipole approximation (DDA) [6], approximation methods, e.g. geometrical optics approximation (GOA) [7], and so on.

The simplest physical model available is the one of a homogeneous dielectric sphere. It was applied to the simulation of cell sizing by using the classical Lorenz–Mie Theory (LMT). It has been successfully used in the sizing of lymphocytes based on the light-scattering signals obtained from a flow cytometer by Neukammer et al. [8]. Nevertheless, this model is very sketchy and takes almost no account of cell morphology or internal structure. To extract more morphological characteristics of lymphocytes from experimental data, a more detailed model is required. The model of a two-layer concentric sphere is proposed by Aden and Kerker [9] and then extended to a multi-layer concentric sphere [10]. These models are much more adequate in the cell diagnosis since the inhomogeneity brought in by the nucleus is taken into consideration. Their advantages are proved in the analysis of nucleated blood cells, for instance, to discriminate abnormal mutated leukocytes caused by virus from normal healthy ones [11]. Also a five-layer model was shown to give a very good agreement between experimental and theoretical light-scattering profiles (LSPs) in the analysis of lymphocyte by Zharinov et al. [12].

Furthermore, through the observation of confocal microscopy, 3D images of a single lymphocyte can be obtained, and one slice of it is presented in the left part of Fig. 1. As we can see, lymphocytes are cells in a nearly spherical shape with clear, transparent cytoplasm and a large single spherical nucleus, which occupies more than 60% of the cell in volume. Additionally, the nucleus suspended within the cytoplasm is not always in the center of the cell. Based on these cellular features of lymphocytes, we could conclude that an eccentric stratified dielectric sphere model approaches to the cell in a greater extent than the concentric stratified sphere model. Nevertheless, due to the complexity of the eccentric sphere model, the calculation of corresponding light scattering problems is not a trivial task. Thus various numerical methods and approximation methods are applied in this study, e.g. finite difference time domain

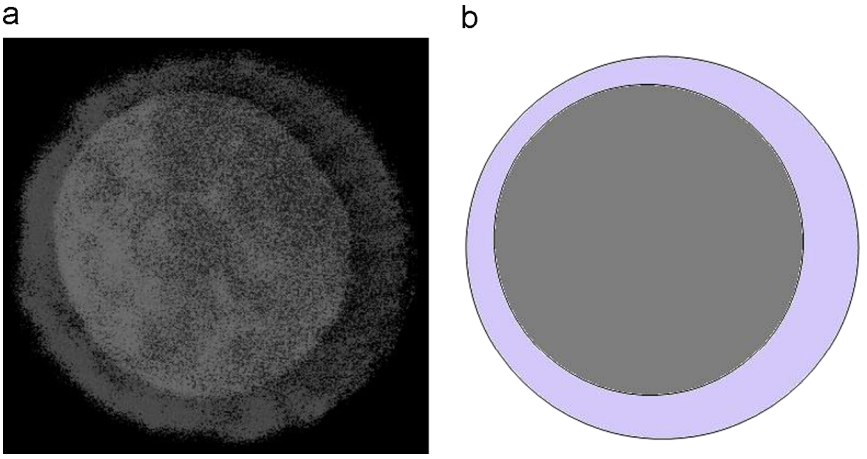

Fig. 1. (a) A slice from a confocal image of a lymphocyte and (b) optical model of a lymphocyte cell with an eccentric core.