Optics and Lasers in Engineering 68 (2015) 93–103

Contents lists available at ScienceDirect

Optics and Lasers in Engineering

journal homepage: www.elsevier.com/locate/optlaseng

An experimental investigation of three-dimensional particle aggregation using digital holographic microscopy

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ARTICLE INFO

Article history:
Received 7 August 2014
Received in revised form
20 November 2014
Accepted 15 December 2014

Keywords:
Three-dimensional microscopy
Three-dimensional image processing
Digital holography
Microscopy
Aggregation

ABSTRACT

The tendency of particles to aggregate depends on particle-particle and particle-fluid interactions. These interactions can be characterized but it requires accurate 3D measurements of particle distributions. We introduce the application of an off-axis digital holographic microscopy for measuring distributions of dense micrometer (2 μm) particles in a liquid solution. We demonstrate that digital holographic microscopy is capable of recording the instantaneous 3D position of particles in a flow volume. A new reconstruction method that aids identification of particle images was used in this work. About 62% of the expected number of particles within the interrogated flow volume was detected. Based on the 3D position of individual particles, the tendency of particle to aggregate is investigated. Results show that relatively few particles (around 5–10 of a cohort of 1500) were aggregates. This number did not change significantly with time.

1. Introduction

The tendency of platelets to clump together at sites of vascular injury, or commonly referred to as platelet aggregation, is important to stop continuous bleeding [1]. This is helped by the formation of thrombus or blood clot in a process known as thrombosis. However, thrombus can also be detrimental in thrombosis when the clots happen to partially or completely block flow of blood through healthy blood vessels, leading to the development of cardiovascular disease [2]. In addition, platelets aggregation is also influenced by the surrounding hemodynamic environments especially in the recirculation and stagnation flow regions and in stenosed micro-channels [3].

Meanwhile, use of therapeutic platelet substitute (e.g. HaemoPlax™) could be an option especially for leukaemic patients to overcome platelet deficiency as a result of undergoing chemotherapy. HaemoPlax™ is based on a proven technology in which a fibrinogen-binding peptide is linked to an insoluble carrier of human albumin through a polyethylene glycol spacer that spatially maximizes binding. On administration, the microsphere is coated in the patient's own inactive fibrinogen and remains inactive until it contacts thrombin, a naturally occurring protein at a site of injury. This contact activates the patient's platelets allowing them to bind to the fibrinogen on the HaemoPlax™ particles, providing an injury site targeted adjunct in patients with insufficient platelet activity. Aggregation prior to activation is clearly undesirable. It is noted that the tendency of particle aggregation depends on particle-particle and particle-fluid interactions. These interactions are closely influenced by the surrounding hemodynamic environments. HaemoPlax™ is stable as delivered, but it has been suggested that high shear rates observed during injection and within the bloodstream could affect coatings and promote aggregation of the particle. The main objective of this study is to experimentally investigate the tendency of therapeutic platelet substitute to aggregate under real blood conditions using digital holographic microscopy.

A new application of holography in the field of optical microscopy has introduced a new imaging technology, known as digital holographic microscopy [4]. Based on the principle of coherence imaging, it allows reconstruction of a three-dimensional (3D) volumetric field from a single hologram capture. The technique relies on digital image and numerical processings to obtain quantitative information in non-invasive and real-time conditions. The essence of holographic imaging lies in the fact that, when coherent light propagates through a semi-transparent object, its amplitude and phase get modulated due to light-matter interaction. This effectively means that the entire 3D structure of the object is coded in the form of scattered wavefronts which eventually incident on to imaging sensors.

Imaging of a relatively low particle concentration is a straightforward process. It however becomes difficult as the particle concentration increases due to noise contributed by out-of-focus particle images [5,6], where the noise severity increases proportional to depth volume [7]. The ability of any digital holographic microscope to detect a number of particles within a system has

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http://dx.doi.org/10.1016/j.optlaseng.2014.12.011
0143-8166/