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Digital holography and image processing methods for applications in biophysics

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Title

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Abstract

Understanding dynamic mechanisms, morphology and behavior of bacteria are important to develop new therapeutics to cure diseases. For example, bacterial adhesion mechanisms are prerequisites for initiation of infections and for several bacterial strains this adhesion process is mediated by adhesive surface organelles, also known as fimbriae. *Escherichia coli* (*E. coli*) is a bacterium expressing fimbriae of which pathogenic strains can cause severe diseases in fluidic environments such as the urinary tract and intestine. To better understand how *E. coli* cells attach and remain attached to surfaces when exposed to a fluid flow using their fimbriae, experiments using microfluidic channels are important; and to assess quantitative information of the adhesion process and cellular information of morphology, location and orientation, the imaging capability of the experimental technique is vital.

In-line digital holographic microscopy (DHM) is a powerful imaging technique that can be realized around a conventional light microscope. It is a non-invasive technique without the need of staining or sectioning of the sample to be observed in vitro. DHM provides holograms containing three-dimensional (3D) intensity and phase information of cells under study with high temporal and spatial resolution. By applying image processing algorithms to the holograms, quantitative measurements can provide information of position, shape, orientation, optical thickness of the cell, as well as dynamic cell properties such as speed, growing rate, etc.

In this thesis, we aim to improve the DHM technique and develop image processing methods to track and assess cellular properties in microfluidic channels to shed light on bacterial adhesion and cell morphology. To achieve this, we implemented a DHM technique and developed image processing algorithms to provide for a robust and quantitative analysis of holograms. We improved the cell detection accuracy and efficiency in DHM holograms by developing an algorithm for detection of cell diffraction patterns. To improve the 3D detection accuracy using in-line digital holography, we developed a novel iterative algorithm that use multiple-wavelengths. We verified our algorithms using synthetic, colloidal and cell data and applied the algorithms for detecting, tracking and analysis. We demonstrated the performance when tracking bacteria with sub-micrometer accuracy and kHz temporal resolution, as well as how DHM can be used to profile a microfluidic flow using a large number of colloidal particles. We also demonstrated how the results of cell shape analysis based on image segmentation can be used to estimate the hydrodynamic force on tethered capsule-shaped cells in micro-fluidic flows near a surface.