OPTOFLUIDIC CHIP WITH SHEET ILLUMINATION FOR HIGH-CONTRAST IMAGING OF FLUID-BORNE MICRO- AND NANO-OBJECTS.

Ghent University is seeking companies interested in commercializing an opto-fluidic chip with sheet illumination through a patent license and/or a collaborative (subsidized) research project.

Introduction

Fluorescence single particle tracking has been shown to be the first technique capable of accurately measuring the size distribution and concentration of fluorescently labelled nanoparticles in undiluted bio-fluids, such as whole blood. However, being based on epi-fluorescence microscopy, a limitation of the technique is the limited contrast due to fluorescence coming from out-of-focus particles or unbound fluorescent dye.

Technology

The proposed opto-fluidic device is a chip with an integrated waveguide which provides sheet illumination in a microfluidic channel containing the measurement sample. This significantly reduces the background noise, resulting in better contrast and detection sensitivity as compared to traditional illumination schemes. Importantly, this device is compatible with lab-on-chip technologies, thus allowing for miniaturized and automated sample analysis.

Applications

One field of application is the characterization of nano-particles in a dispersion. For example, the opto-fluidic chip can be used for characterization methods based on single particle imaging. The current technique can be used both for clear liquids (light scattering and fluorescence mode) and biological fluids (fluorescence mode) such as blood. As another example, the opto-fluidic chip could be used to acquire optically sectioned images of micro-objects, such as biological cells. Relevant application areas are:

- Characterization of nano-medicines for drug delivery
- Protein aggregation in drug formulations
- Characterization of endogenous nanoparticles for biomedical diagnostics
- Characterization of nanoparticles for biomedical imaging
- Study of additives in oil and petro-chemistry
- Detection and characterization of virus like particles
- Imaging flow cytometry

Advantages

- By illuminating the sample in a thin plane coinciding with the focal plane, the background noise is significantly reduced, resulting in improved contrast and detection sensitivity.
- The measurement channel of the chip has a small volume, thus reducing the sample size.
- Miniaturization and automation of measurements
- Integration with other lab-on-a-chip measurements
- Possibility to manufacture as a low-cost disposable

State of development

We have produced a mass-manufacturable microfluidic chip with integrated light sheet illumination, and demonstrated that it allows accurate fluorescence single particle tracking size and concentration measurements of membrane vesicles in cell culture medium and in interstitial fluid collected from primary human breast tumors.

Partnership

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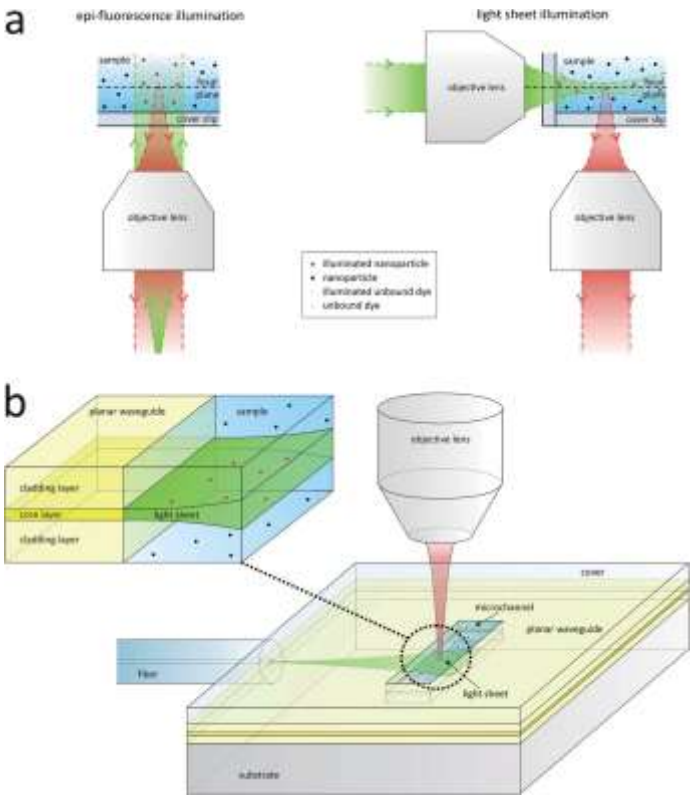
Intellectual property

Patent title: Methods and systems for optical characterization
European patent application EP2513628
Granted US patent US8928875

Figure



Microfluidic chip with integrated waveguide for light sheet illumination
(a) Illustration of the (green) excitation and (red) fluorescence light path in epi-fluorescence and light sheet illumination. The contrast for the nanoparticles in focus is better with light sheet illumination because the nanoparticles and unbound dye out of focus are not illuminated.
(b) Design of a microfluidic chip with integrated waveguide for on-chip light sheet illumination. Laser light enters the planar waveguide by means of an optical fiber. While the laser light is confined in the vertical direction, it can spread horizontally in the waveguide so that a sheet of light emerges in the microchannel. The fluorescence light is collected by an objective lens whose focal plane coincides with the light sheet. The drawing is not to scale.

References

On-chip light sheet illumination enables diagnostic size and concentration measurements of membrane vesicles in biofluids. Deschout et al. Nanoscale 2014, 6, 1741

Keywords

Micro-fluidic, chip, sheet illumination, micro-particle, nano-particle, concentration, fluorescence, lab-on-chip

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