TIME AND POSITION DEPENDENT SURFACE FLOW VELOCITY MEASUREMENT IN MICROFLUIDIC DEVICES

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ABSTRACT 100 words

We have developed a simple method for measuring surface flow velocity inside a microfluidic channel. Tracking the refractive index boundary in the flow channel gave the flow velocity. The refractive index boundary was measured by surface plasmon resonance (SPR), thus our method gave both the physical flow condition and biological interaction information in a single sample run. In our previous attempt, we required the shape of the boundary to be predefined for tracking. In this report, we introduce a 2D Fourier transform based algorithm where no predefined shape is required for tracking, and we test its capability with a milk sample.

KEYWORDS

Flow velocity, surface plasmon resonance, refractive index, Fourier transform

INTRODUCTION

The flow velocity in a microchannel affects the mixing efficiency and reaction rate, and is affected by the channel shape and flowing liquid properties. In a biological interaction assay that of an immobilized antibody and antigen in a sample, we need to consider the mass transport caused by flow and diffusion (represented by the Péclet number) in this heterogeneous reaction at the microchannel wall in order to design the optimum flow condition in terms of sensitivity and the dynamic range of the assay [1]. Therefore, flow velocity measurement methods have been widely studied [2]. However, most methods require us to mix marker particles and to use special optical setups that are not suitable for use with biological assays.

By contrast, there has been an increasing demand for a simple and easy biological assay technique for healthcare, agriculture, and food industry applications. We have developed a surface plasmon resonance (SPR) and microfluidic device based immunoassay system to meet these demands [3-5]. We used a small sized SPR instrument and a capillary force self-pumping microfluidic system equipped with an antibody array. This system can detect multiple target molecules with an antibody array immobilized in the microfluidic device. For this system, we have developed an in-situ method to measure the surface flow velocity in the microfluidic device to compensate for the unstable flow rate of the self-pumping system.

Here, we report the extended capability of surface velocimetry for microfluidic devices. The previous method [6] required a single sharp liquid-liquid boundary, and was limited to determining the average velocity of the entire flow through time and streamwise length.

We introduce a new algorithm for measuring variations in time and the internal flow velocity and employ a sample injection microfluidic circuit that shapes the liquid-liquid boundary and thus alleviates the boundary shape restriction. We tested this method in an immunoassay application using a milk sample and were able to measure the flow velocity variation. Our method can be applied to a wide range of sensors and provide hydrodynamic information about samples. It will also provide practical nano-scale surface velocimetry for the investigation of such liquid behavior as unsteady flow, and the slipping and adhesion of molecules to the walls of microfluidic devices.

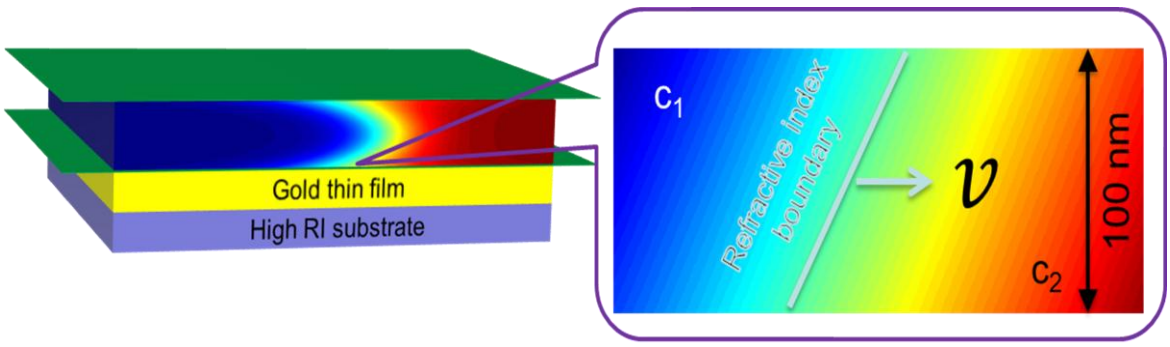

Figure 1. Principle of surface velocimetry. The moving velocity of the refractive index boundary was directly measured by SPR. The velocity reflects both the movement of liquid and the diffusion of liquid molecules with a low Péclet number (<100).

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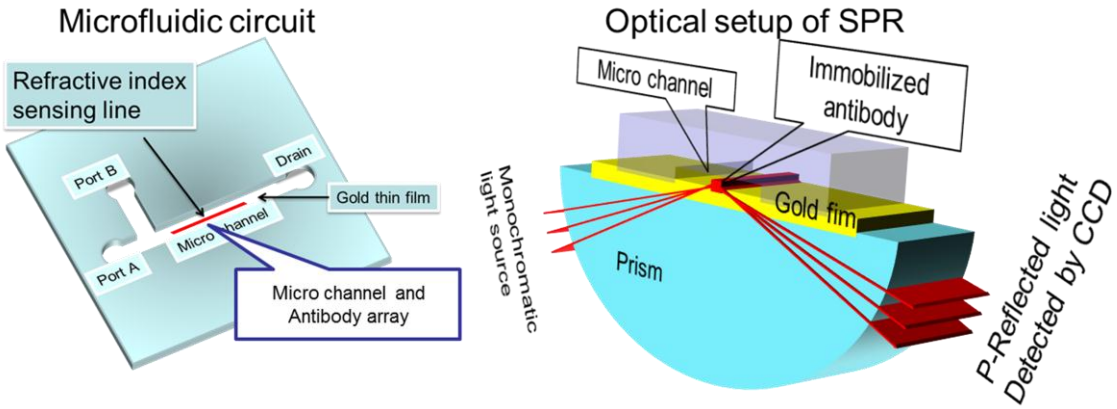

Figure 2.Pattern of microfluidic circuit, and optical setup of spatiotemporal RI measuring SPR instrument.

RESULTS and DISCUSSION

Our velocimetry approach is based on tracking the RI boundary of two sequentially injected sample liquids (Fig. 1). First, the refractive index (RI) boundary is detected using a piecewise 2D Fourier transform (2DFT) from the RI map (Fig. 3). Because any patterns moving at the same speed in Fig. 3 are converted to a line crossing the origin by the 2DFT, unclear boundary lines and multistep boundary segments can be detected. This enable us to detect the position dependent flow velocity while a real sample (milk) was flowing. We adopted this algorithm from μPIV technology, not for the particle trajectory, but for the near-field RI data. Because the RI directly measures the flow velocity including the diffusion of the liquid constituent, our method provides undisturbed real flow conditions. Second, we designed an optimized microfluidic circuit to realize a clear liquid-liquid junction, and the RI boundary was formed just in front of the SPR observation area. This circuit is compatible with any immunoassay device with an antibody array, and it is ready for use as a sensor device.

The spatiotemporal RI (Fig. 4 upper panel) was measured with a simple small surface plasmon resonance (SPR) instrument (Fig. 2) that could measure the RI of the 4.8 mm streamwise length of the microfluidic device with 10-μm resolution. The lower panel in Fig. 4 shows the result of the milk (containing antigen) sample injection. Although the RI map of the milk sample showed RI noise, the algorithm in Fig. 3 can utilize these effectively to calculate velocity. The present method is simpler than other methods (PIV, XRD, NMR) [2]. Therefore, this velocimetry will also accelerate the realization of POCT and rapid biological tests in the food industry.

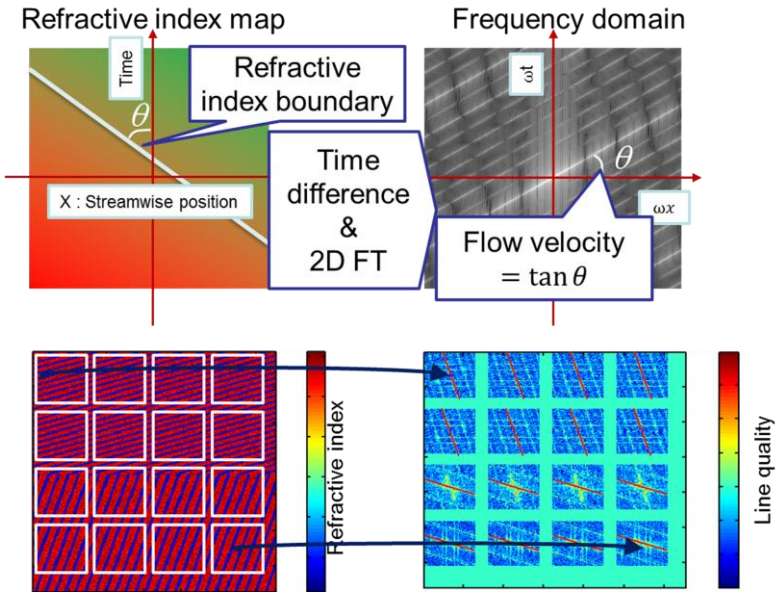

Figure 3. Principle of refractive index boundary detection using 2D Fourier Transform. The slope of RI represents the flow velocity. Any RI boundary pattern showing the same slope in the RI map is converted to a line crossing the origin by the transform. This transform was performed piecewise.

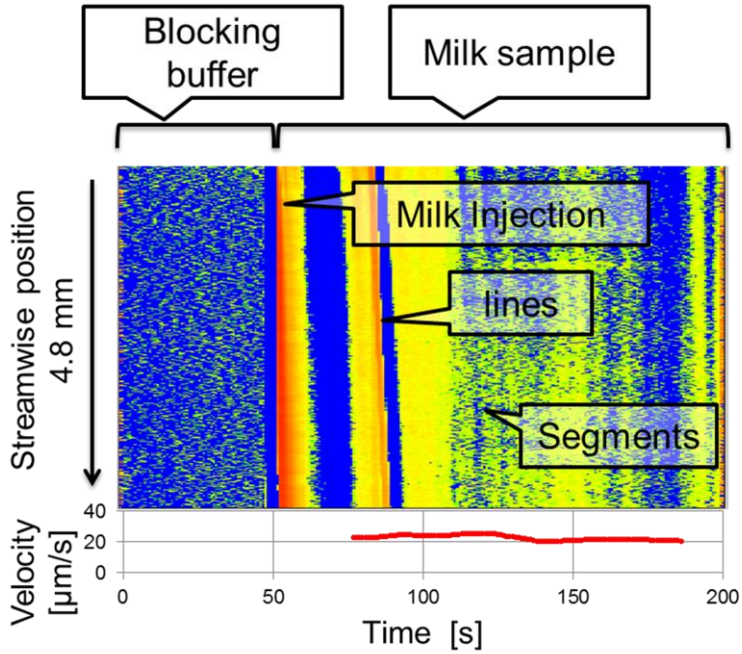

Figure 4. Flow velocity measurement of a milk sample with a capillary force driven microfluidic device. In the RI map (x is time, y is streamwise position, z is the time differential of the RI shown in color) many RI boundary lines and segments were observed because of the complex milk constituents. These were not observed when there was a flow of blocking buffer. The flow velocity could be calculated at any position after injecting the milk sample by using the algorithm in Fig. 3.

Because the Péclet number (hydrodynamic/diffusional length ratio) is small (~100) under our and other immunoassay conditions, the flow velocity is strongly influenced by diffusion [2]. Therefore, the RI boundary became unclear as the flow moved downstream, and this hampered the applicability of this velocimetry approach. The two new techniques introduced here improved the velocity measurement accuracy and measurement versatility.

Using the new algorithm, we could confirm the injection of the correct sample and detect a stacked flow. Moreover, we could also use the hydrodynamic properties of the sample in addition to its molecular biological properties to assess the safety of a food sample. We could verify and validate the test result from the sensor, whose malfunctioning could lead to mistakes in the subsequent diagnosis and treatment. Therefore, a validation mechanism is necessary for an end user operating a sensor system. These applications also require the end user to apply samples directly to the sensing devices without pretreatment of samples. Therefore, the physical properties of sample liquids varied in viscosity and unexpected contaminants including mistakenly collected samples and cloggy samples. Flow condition monitoring will also solve these problems.

REFERENCES

[1] "Analysis of Macromolecular Interaction Using Immobilized Ligands," I. Chaiken, S. Rose, R. Karlsson, Anal. Biochem., 201, 197-210 (1992)

[2] "Chapter 4 Experimental Flow Characterization, in Fundamentals and Applications of Microfluidics," N.-T. Nguyen, S. T. Wereley, Artech House, (2002)

[3] *"Passive Fluidic Chip Composed of Integrated Vertical Capillary Tubes Developed for On-Site SPR Immunoassay Analysis Targeting Real Samples,"* T. Horiuchi, T. Miura, Y. Iwasaki, M. Seyama, S. Inoue, J. Takahashi, T. Haga, E. Tamechika, Sensors 2012, 12(6), 7095-7108.

[4] "Quick and Simple Measurement for Antibody Array in Disposable Microfluidic Devices Using Surface Plasmon Resonance," Y. Iwasaki, T. Horiuchi, M. Seyama, T. Miura, E. Tamechika, Proc. The 4th International Symposium on Microchemistry and Microsystems., 239 (2011).

[5] "Patterned cellulose membrane for surface plasmon resonance measurement," T. Miura, T. Horiuchi, Y. Iwasaki, M. Seyama, S. Camou, J. Takahashi, T. Haga, Sensors & Actuators: B. (2012) in press.

[6] "In-situ Sub-micrometer Surface Flow Velocity Measurement," Y. Iwasaki, M. Seyama, T. Miura, T. Horiuchi, E. Tamechika, Proceedings of microTAS 2011.

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