UNIDIRECTIONAL SHAKE-MODE FOR MIXING HIGHLY WETTING FLUIDS ON CENTRIFUGAL PLATFORMS

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ABSTRACT

We present a novel approach for washing and mixing on centrifugal microfluidic platforms. Mixing and washing are essential unit operations for lab-on-a-chip platforms but often cause valving problems if they are performed with "real life fluids" like washing buffers containing high detergent or salt concentrations which are often used in diagnostic or biological assays. We therefore improved the shakemode mixing technique to find a method that combines reliable siphon-based valving with high mixing and washing efficiency. Therefore the so called unidirectional shakemode, is introduced and correlated to the already established technologies.

KEYWORDS: Centrifugal Microfluidics, Mixing, Washing, Siphon Valving

INTRODUCTION

For centrifugal microfluidic platforms[1] one of the most effective methods for washing, mixing and dissolution of prestored reagents is a frequent inversal of the spinning direction (fig.1A), called shakemode [2,3]. This shakemode process is often combined with fluidic structures that use siphon valves for fluid routing. Siphon priming is avoided by spinning the lab-on-a-chip leading to domination of the centrifugal force over the capillary force pointing in the opposite direction (fig. 2A). Inevitable, every inversion of the spinning direction causes the siphon to fill a bit because a critical spinning frequency is underrun leading to domination of the capillary force. This phenomenon is deteriorated if fluids with a low surface tension like washing or lysis buffers are used that provoke capillary siphons to brake within seconds.

Our novel technique allows efficient mixing and washing without affecting the functionality of siphon valves. To achieve this we accelerate and deccelerate our lab-on-a-chip while spinning is performed in only one direction. If the spinning frequency is kept over a critical frequency (fig. 1B), breaking of capillary and volume triggered siphon valves can reliably be avoided.

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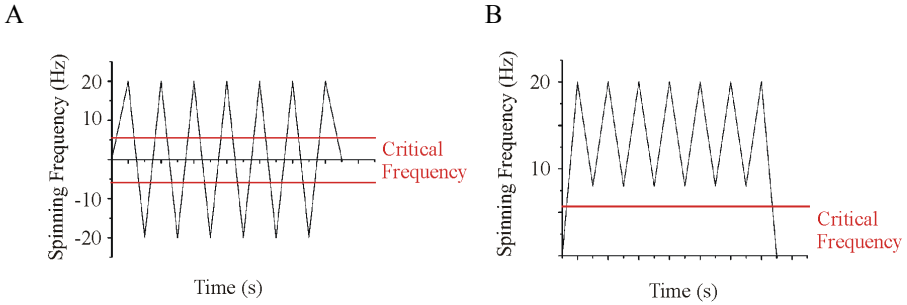

Fig. 1: A) Frequency protocol of a bidirectional shakemode. The critical frequency, in which the capillary force is higher than the centrifugal force, is underrun each time the spinning direction changes. B) The frequeny protocol of the unidirectional shakemode shows that the spinning frequency is higher than the critical frequency all the time.

EXPERIMENTAL RESULTS

To proof the compatibility of unidirectional shakemode mixing with capillary siphon valves we investigated the stability of these siphons under assay conditions with our mixing protocols. 50 µL of washing buffer (PBS, 0.1 % Tween 20) is added into a chamber with an interconnected capillary siphon that is coated with polyethylenglycol (PEG) resulting in surface hydrophilization. Using a bidirectional shakemode the siphon valve breakes after 8s leading to draining of the chamber. If the unidirectional method is performed the siphon doesn't break even after 3 hours, allowing long-term mixing, incubation or washing steps.

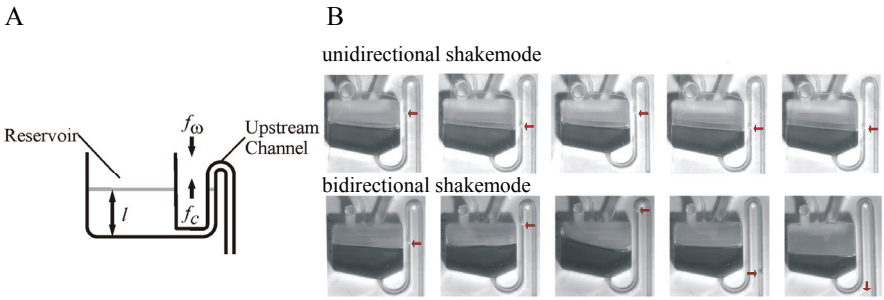

Fig. 2: A) Schematic drawing of a siphon valve. If the centrifugal force dominates over the capillary force the reservoir won´t drain. B) With a shakemode protocol the filling level of washing buffer in the siphon raises due to temporary domination of the capillary force. The siphon valve breaks after 8s and the reservoir empties into an interconnected chamber. Performing an unidirectional shakemode the filling level of the siphon varies with the spinning frequency but the siphon doesn't break even after a timespan of three hours.

Figure 3A shows pictures of mixing experiments. The time it takes to mix two fluids, in this case 2 µL ink and 50 µL DI-water with a unidirectional shakemode is below three seconds, proving the efficiency of this mixing method. A correlation of washing techniques is presented in figure 3B. The experiments show that the removal of Cy5-labelled biotin molecules adhesively coupled to a PS-substrate due to washing after 3 washing steps is equal for all benchmarked techniques.

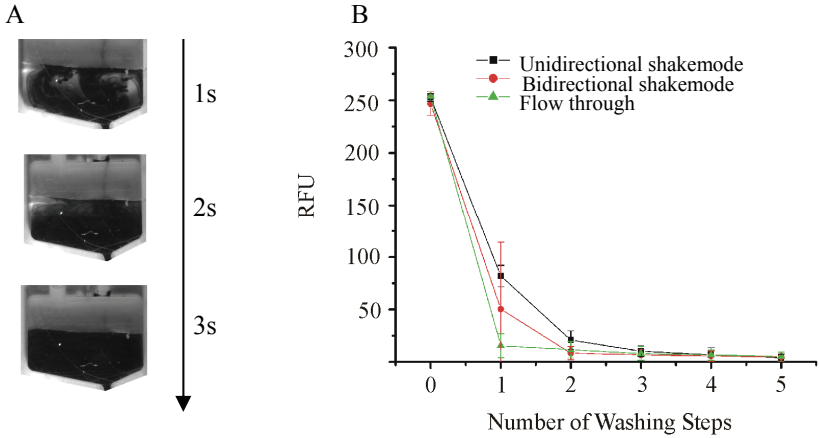

Figure 3: A) The mixing efficiency of the unidirectional shakemode is demonstrated with 2 µL ink in 50 µL water. Homogeneous mixing occurs after 3 seconds. B) The graph shows a comparison of washing techniques available for centrifugal lab-on-a-chip systems. For this experiments Cy5-labelled biotin is immobilized due to adhesion on a PS-substrate and the fluorescence signal is measured prior to washing and after each washing step. After the first wash flow through - and shakemode washing show the lowest fluorescence signa. After 2 washing steps the fluorescence signal for all washing techniques is equal.

CONCLUSIONS

We present a novel approach for washing and mixing on centrifugal microfluidic platforms specialized on applications with detergents and salt containing fluids. Our technology allows efficient mixing and washing without affecting the stability of siphon valve-based fluid routing. This enables the integration of new and more complex diagnostic and biological assays in centrifugal lab-on-a-chip systems.

ACKNOWLEDGEMENTS

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