DISC-EMBEDDED GRINDING MILL TOWARDS PROCESS INTEGTRATED HYDRO-MECHANICAL CELL LYSIS ON CENTRIFUGAL MICROFLUIDIC PLATFORMS

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ABSTRACT

For the first time we utilize the spindle motor intrinsic to centrifugal microfluidic systems to drive a grinding mill for cell lysis in a stator-rotor concept. This mechanical concept particularly enables the lysis of armored cells and, as a further benefit, avoids the addition of chemicals that potentially inhibit subsequent reactions. As a proof of concept we demonstrate the lysis of the silica-shelled algae *Phaeodactylum Tricornutum*.

KEYWORDS: Mechanical cell lysis, Centrifugal microfluidics, Stator rotor.

INTRODUCTION

Cell lysis is the first step in cell content analysis, e.g. for nucleic acids or proteins. On centrifugal microfluidic platforms, this procedure has been implemented by conventional chemical methods [1] or centrifugo-magnetically actuated bead milling [2]. Inspired by the work of Millis *et al.* [3], we have developed a purely mechanical cell lysis mechanism constituted by a concentrically held stator ring as a grinding surface used to shear open the cell wall.

EXPERIMENTAL

The system in Figure 1a consists of a 120-mm diameter disc assembled from three PMMA layers which are interspersed by structured films of pressure-sensitive adhesive (PSA). A 2-mm thick PMMA annular stator exhibiting a roughened underside is embedded within the setup. The disc consists of two loading chambers connected via channels on the bottom PSA layer to the bottom side of the stator ring (Fig. 1b). Four collection chambers are evenly spaced at the periphery of the disc. For mechanical fixing by pins, the stator ring contains two holes, while the main disc can freely spin. The holder is assembled by four parts (Fig. 1d): an upper mount, a lower mount and two PMMA sections. The PMMA sheets are screwed to the metal box surrounding the spindle motor. The clear PMMA sheets allow optical inspection of the collection chambers.

RESULTS AND DISCUSSION

A 500-µL suspension of the cells is introduced into each of the loading chambers. Under rotation the centrifugal field pumps the liquid from the loading chamber through the small gap below the stator to lyse the cells by hydro-mechanical shearing of their walls (Fig. 1c). The efficacy of lysing algae was assessed using a traditional cell counting chamber on a microscope (Fig. 2). Already after a single pass through the grinder, a ~30% decrease in cell density was observed and the fluorescence signal significantly increased with respect to the pre-lysed sample.

CONCLUSION

Future work will aim to improve the lysis efficiency of the system by modifying its parameters, such as the raster depth and pattern on the stator, and the rotational frequency. We will then integrate the grinder for upstream lysis in a fully sample-to-answer automated cell content analysis procedure on the “Lab-on-a-Disc” platform.

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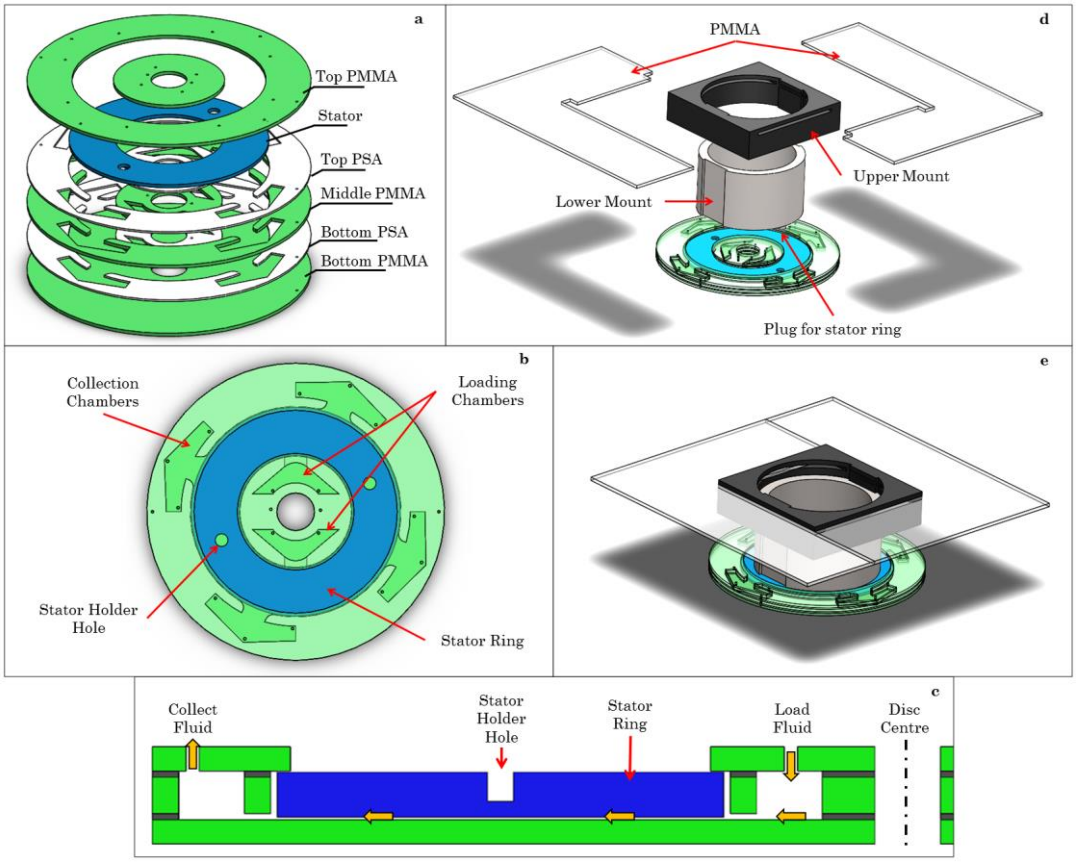

Figure 1: Functional components of stator rotor. a) Exploded view of stator rotor disc design. The disc consists of three 1.5-mm thick PMMA layers (green) held together by two 86-µm thick PSA films (white). The 2-mm thick, annular PMMA stator (blue) featuring a roughened bottom surface is embedded within the device. b) Top down view of disc design. c) Cross-sectional view of system design. Yellow arrows indicate the direction of fluid flow. d) Exploded view of the functional components of the stator rotor holder. Upper and Lower Mounts are 3D printed and the 3-mm thick PMMA sheets are cut using laser ablation. e) Assembled view of the holder.

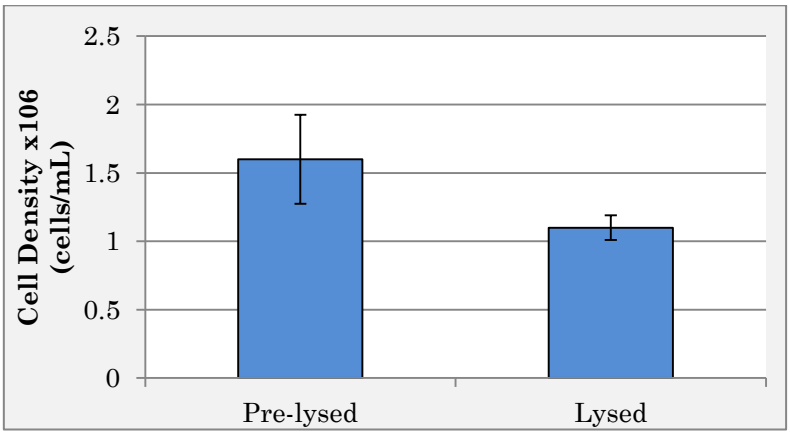

Figure 2: Comparison of pre-lysed and lysed algae samples. The cell density decreased by approximately 30% after the cells were passed through the system. Data points are mean ± 1 standard deviation, n=3.

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