Optical Fiber-Based Module for Selection and Picking of Cells and Cell Clusters

A. V. Harish[1, *, †], Joao Varela[2, †], Timothy Gibbon[3, *], Walter Margulis[3, *], Aman Russom[2, *], and Fredrik Laurell[1]

[1]Laser Physics Group, Department of Applied Physics, KTH Royal Institute of Technology, Stockholm, Sweden
[2]Division of Nanobiotechnology, Department of Protein Science, Science for Life Laboratory, KTH Royal Institute of Technology, Solna, Sweden
[3]Research Institutes of Sweden (RISE), Stockholm, Sweden
[†]Authors have contributed equally

Abstract. We have developed an optical fiber-based module that can select, retrieve, and transfer single cells, and cell clusters. Cell picking and isolation has several applications such as separating circulating tumor cells, isolating single fetal cells for prenatal testing, and others. Our Lab-in-a-Fiber (LiF) module can detect fluorescent cancer cells (MCF-7) from a mixture of labeled and unlabeled cells and pick them up for further analysis. The cells picked up by the fiber show a 90% survival rate on viability tests, making this cell-picking technique an attractive alternative to existing methods.

1 Introduction

Fiber optic technology carries enormous potential for use in medical diagnostics and therapy [1], already being heavily used for imaging (endoscopes) [2], biosensing [3, 4], and optical coherence tomography [5]. Further functionalization of optical fibers has resulted in the emergence of a new concept: "Lab-in-a-Fiber" (LiF) technologies [6, 7]. This fiber-optic counterpart to the "Lab-on-a-Chip" (LoC) technology, mostly focused on life science applications, has ever since revolutionized the field of medicine.

Optical fibers can also be combined with other technologies, namely LoC, to improve the performance of various diagnostics methods. For example, a LoC microflow cytometer was recently demonstrated using optical fibers to deliver and collect light to and from the chip [8]. Several attempts have been made to make flow cytometers with LiF technology [9]. A LiF device to detect circulating tumor cells with a fiberoptic probe using multiphoton flow cytometry [10] has been developed, showcasing the growing influence of fiberoptic technology in life science. Our group has previously also demonstrated a microflow cell separation and counting which uses optical fibers and silica capillaries [11]. In previous work, we developed a LIF device capable of selectively picking up fluorescent beads from solutions [12].

Here, we present a LiF device capable of selectively picking up cells from a petri dish based on their fluorescent signal. The capture and isolation of individual cells or small clusters, an important aspect in biomedical analysis, would allow an accurate diagnosis of various diseases, namely different cancer types.

2 Experimental Setup and Results

Our LiF device consists of two fibers that are rolled into a single unit. One of the fibers is a multimode fiber used to excite and collect light. The other is a silica fiber capillary with 90 µm inner diameter and 125 µm outer diameter (90/125 µm capillary). After stripping these fibers to remove the jacket they are inserted in a 255/330 µm housing capillary. We etch the inside by flowing hydrofluoric acid to increase the inner diameter to 260 µm for ease of insertion into the housing capillary. To secure the fibers in the desired position, the housing capillary was flooded with sodium silicate (2.5 mol%) water and air-cured. Subsequently, the tip of the LIF component was diced using a high-speed diamond saw and then treated with hydrophobic liquid to avoid cells adhering to the walls of the fiber capillary. A cross-section image of the LIF device is shown in the inset of Fig. 1. For conducting the experiments, MCF-7 cells were acquired and cultured in Dulbecco's modified Eagle's medium-F12 (DMEM; Sigma-Aldrich) supplemented with 10% Fetal Bovine Serum (FBS; Sigma-Aldrich) and 1% penicillin-streptomycin 100 U/mL (Sigma-Aldrich), in a humidified incubator with 5% CO_2, at 37°C. Once confluency of 70-80% was reached, the cells were incubated with a solution of Calcein-AM (2.5 µM; Sigma-Aldrich) for 20 minutes, and subsequently dissociated and collected from the cell culture flask using a 0.25% solution of Trypsin-EDTA

* Corresponding author: harishav@kth.se

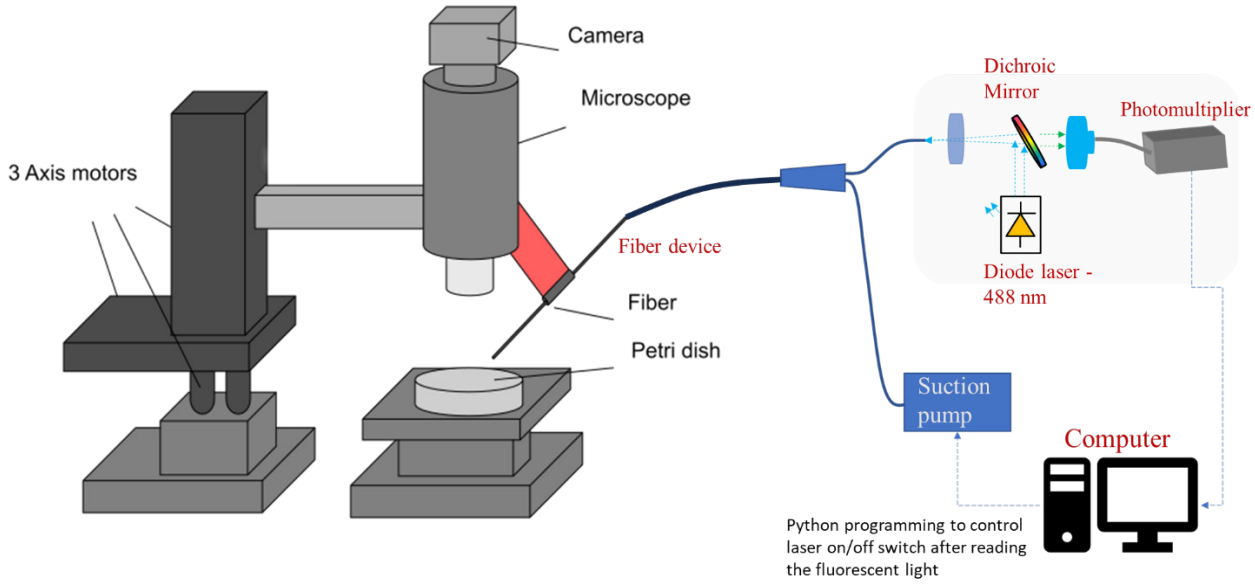

Figure 1 Schematic diagram of our experimental setup showing the Lab-in-a-fiber device, diode laser, fluorescence measuring setup, and 3D stage on which the fiber is mounted and connected to a PC for control. of the setup. Inset pictures show the cross-section image of the LiF component.

(Sigma-Aldrich), followed by centrifugation at 1300 rpm for 5 minutes. The cells were then resuspended in either DMEM or phosphate-buffered saline (PBS) solution and diluted to the desired concentration. The fiber probe was mounted on a 3D stage and used to search for green, fluorescent cells in the petri dish. A 488 nm fiber-coupled diode laser (pulse modulated [13]) was used to illuminate the solution in front of the fiber tip. The component could either be scanned through the liquid controlled by a computer program or manually swept through the solution

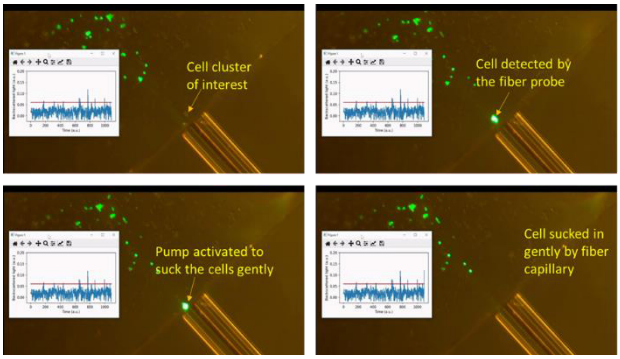

Figure 2 The tip of our device illuminating a fluorescently tagged cell in a petri dish before it is sucked into the fiber capillary.

using a joystick. When a labeled cell was illuminated, the fluorescence signal was momentarily collected via the MMF, separated via a dichroic mirror, and detected. The signal triggered a vacuum pump, applying negative pressure to the capillary, and the cell was then collected. The successful collection of cells shows the potential of this component for clinical settings, where for example cancer cells could be collected for in-vitro analysis. Furthermore, the possibility of combining this component with other technologies for quick downstream analysis may allow for local, precise point-of-care diagnosis and treatment.

We thank the Swedish Research Council (Vetenskapsrådet) for funding this collaborative research work with research grant number 2021-03413.

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