

# An Integrated Single Cell Optofluidic Platform Based on Phototransistor Optoelectronic Tweezers

Arash Jamshidi<sup>1</sup>, Justin K. Valley<sup>1</sup>, Wilbur Lam<sup>2,3</sup>, Hsan-Yin Hsu<sup>1</sup>, Tiffany Dai<sup>1</sup>, Sharmin Shekarchian<sup>1</sup>, Steven L. Neale<sup>1</sup>, Shao Ning Pei<sup>1</sup>, and Ming C. Wu<sup>1</sup>

<sup>1</sup>Berkeley Sensor & Actuator Center and Department of Electrical Engineering and Computer Sciences, University of California, Berkeley.

<sup>2</sup>Department of Pediatric, University of California, San Francisco <sup>3</sup>Department of Bioengineering, University of California, Berkeley, USA

Contact e-mail: arash@eecs.berkeley.edu

**Abstract:** We present a novel single cell manipulation platform based on phototransistor optoelectronic tweezers. This new platform integrates the functionalities of phOET for parallel cell manipulation in highly conductive culture media with a commercial microfluidic device.

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## 1. Introduction

There has been a growing interest in microfluidic platforms for reliable handling of individual cells and control of their biological environments. However, most commercial devices are passive, meaning that they lack the capability to interact with and manipulate single cells. Optofluidic technologies have played an important role in handling of single cells for quantitative biological studies. However, these techniques (including optical tweezers) require the use of complicated and expensive optical setups which complicates their integration with existing microfluidic platforms. Optoelectronic tweezers [1] (OET) has recently emerged as a powerful technique for large-scale and real-time manipulation of micro- [1] and nanoscale [2] particles. OET is capable of manipulation of single cells over working areas  $>1\text{mm}^2$  using commercial light projectors ( $<10\text{ W/cm}^2$  optical intensity). Even though the conventional OET is limited to operation in low conductivity medium ( $<100\text{mS/m}$ ), a novel OET device called phototransistor OET (phOET) [3] overcomes this challenge using an N<sup>+</sup>PN phototransistor structure as the photoconductive material allowing single cell manipulation in high conductivity physiological solutions ( $>1\text{ S/m}$ ) which is essential to maintaining cell viability. The relaxed optoelectronic actuation requirements for OET device makes it an attractive choice for integration with commercial microfluidic platforms to achieve active manipulation of cells. In this paper, we demonstrate the integration of phOET device with a commercial microfluidic platform to achieve active parallel manipulation of single cells in culture conditions with translation speeds exceeding  $20\mu\text{m/s}$ .

## 2. Integration of Phototransistor OET (phOET) with a Commercial Microfluidic Platform

The commercial microfluidic platform used here for integration with phOET is Frochet Chamber System 2 (FCS2 from Bioptechs Inc.) [4]. FCS2 is a closed flow chamber for real-time observation and monitoring of cells combined with thermal control and laminar flow perfusion of cell medium. Figure 1 shows the experimental setup used to actuate the phOET device integrated with FCS2 system. The inset of figure 1 shows the side view cross section of the phOET device integrated with the FCS2 system. The fluidic chamber is locked between a bottom metallic base and a top piece. A plastic chip carrier is used to hold a  $0.9\text{cm}\times 0.9\text{cm}$  phOET chip and silicone adhesive is used to seal the gaps around the chip, silver epoxy is applied to the bottom of the chip to make a backside electrical connection. To form the fluidic chamber, a rubber gasket (0.25 mm thick) is used to separate the bottom phOET chip surface from a top glass slide coated on both sides with indium tin oxide (ITO). The top glass slide also has two T-shape grooves which interact with the perfusion lines to bring the liquid medium in and out of the chamber.

The assembled phOET chamber is locked between the metallic base and the top piece and electrical connections are made to the ITO layer inside the chamber (through vias on the top piece) and the backside connection. A home-built microscope is used for observation, time-lapsed imaging, and phOET optical actuation by focusing light patterns from a commercial light projector (controlled using a Powerpoint interface) onto the phOET device. An ultra-low flow peristaltic micro-perfusion pump is used to perfuse the culture solution into the chamber. The cells are introduced through a syringe by temporarily switching the perfusion line. Once the cells are inside the chamber, they can be manipulated using the phOET device integrated inside the chamber. The maximum translation speed of trapped cells exceeds  $20\mu\text{m/s}$  (corresponding to a 2pN dielectrophoresis force) and the optical traps can be used to hold cells in place during the perfusion of cell media. A temperature controller is used to keep the chamber temperature at  $37^\circ\text{C}$ . However, the application of AC voltage increases this temperature by  $\sim 4^\circ\text{C}$  (monitored at the top of the chamber); this temperature increase is reduced to  $\sim 0.7^\circ\text{C}$  by using a bottom silicon layer to provide better heat sink. Moreover, the initial temperature set point can be adjusted to a lower value to offset this temperature increase. Figure 2 shows parallel manipulation of single HL60 cells (human leukemia cells used to model acute

myeloid leukemia) to form a  $2 \times 2$  array. The manipulation is performed in standard RPMI media in 10% fetal bovine serum using a 10Vpp at 1 MHz AC voltage source. Once the four HL60 cells are trapped, they can be moved in parallel through translation of optical traps. This level of single cell control combined with commercial microfluidic devices opens up the possibility for various quantitative biological studies such as long-term (1-2 weeks) single-cell monitoring in culture conditions and live-cell imaging over multiple cell generations.

### 3. References

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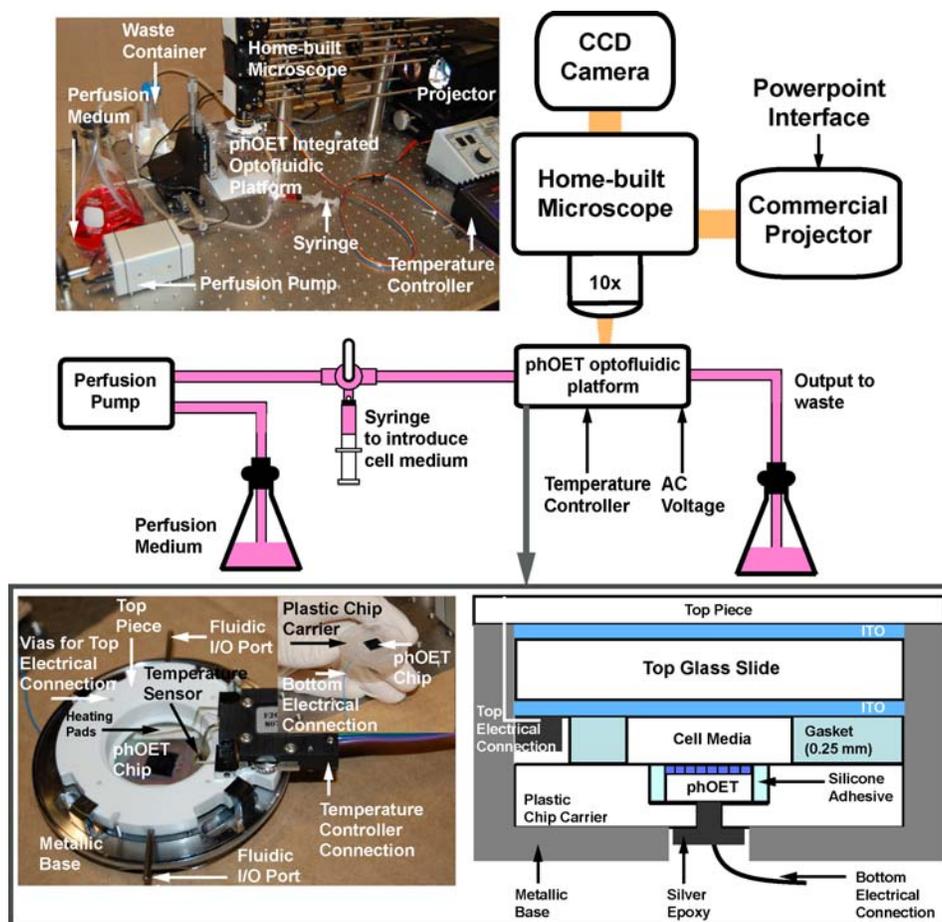


Fig. 1: An overview of the setup for cell culture media perfusion, optical actuation, and temperature control of the integrated phOET microfluidic platform. The inset shows side-view schematic and assembled device image of phOET integrated with FCS2 microfluidic chamber.

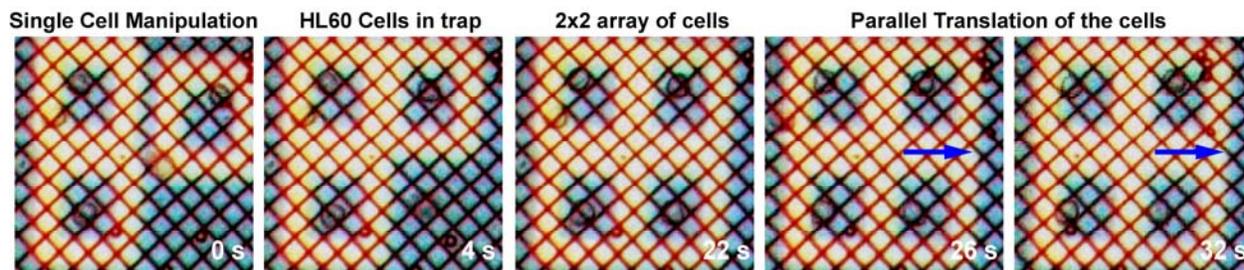


Fig. 2: Parallel manipulation of single HL60 cells using phOET microfluidic platform. A  $2 \times 2$  array of HL60 cells is formed using light patterns projected onto the phOET device inside the microincubator chamber to trap the cells. Once the array is formed, the cells are translated simultaneously by moving the light patterns.