Supplemental information

Continuous Nucleus Extraction by Optically-Induced Cell Lysis on a Batch-type Microfluidic Platform⁺

Shih-Hsuan Huang^a, Lien-Yu Hung^a and Gwo-Bin Lee^{a, b, c*}

^aDepartment of Power Mechanical Engineering, National Tsing Hua University, Hsinchu, Taiwan 30

^bInstitute of Biomedical Engineering, National Tsing Hua University, Hsinchu, Taiwan 300

^cInstitute of NanoEngineering and Microsystems, National Tsing Hua University, Hsinchu, Taiwan 300

I. Non-treatment control of OICL test and parameters of transmembrane potential



Supplemental Figure S1: Illustration of the cell membrane lysis into the integrated OICL chip by using optically-induced multi-spot light. (a) \sim (d) A series of photographs to show the cells before OICL. (e) \sim (h) A series of photographs to show the cells after OICL

The transmembrane potential of a cell under an AC electrical field could be modelled by the Schwan equation in an AC field.

$$\Delta \psi_{membr} = \frac{1.5 \ a \ E_{appl} \cos \theta}{\left(1 + \left(\omega_{ac} \tau\right)^2\right)^{1/2}}$$

$\Delta\psi_{membr}$	Transmembrane potential (V)	
θ	Angle between field line and the normal to the point of interest	
E _{appl}	Applied electric field	
а	Outer cell radius (µm)	
ω _{ac}	Angular frequency of applied field (rad/sec)	
C _{membr}	Capacitance of the membrane (F/cm ²)	
$ \rho_{int} $	Resistivity of the internal fluid ($\Omega \cdot cm$)	
$ \rho_{ext} $	Resistivity of external medium (Ω ·cm)	

Supplemental Table S1: Definitions of the parameters of transmembrane potential



Supplemental Figure S2 : Schematic illustration of the cell lysis process. (a) The transmembrane potential was produced because of exposure to an optically-induced electric field. (b) If the transmembrane potential exceeded the critical threshold value, the cell's membrane would be permeabilized, could even be lysed.

II. Calculation of ODEP drag forces

Stokes' law describes the drag force (F) that is exerted on a spherical particle in a continuous flow condition, and can be expressed as equation (1).

$$F = 6 \pi rgv \qquad (1)$$

where r, g, and v denote the radius of cells, the viscosity of the fluid, and the terminal velocity of the cells, respectively. In this study, the manipulated cells were attracted to attach to the bottom surface of the cell manipulation zone. For a better approximation, the above Stokes' law was modified according to the Faxen's correction. It mainly describes the hydrodynamics of a single sphere near a rigid planar surface, which could be expressed as equation (4).

$$F_{\rm drag} = \frac{6\pi r \eta v}{\left[1 - \frac{9}{16}\left(\frac{r}{h}\right) + \frac{1}{8}\left(\frac{r}{h}\right)^3 - \frac{45}{256}\left(\frac{r}{h}\right)^4 - \frac{1}{16}\left(\frac{r}{h}\right)^5\right]}$$
(2)

where h represents the distance from the surface to the center of a biological cell. In this study, h was thus assumed to be the radius of the cells. At a given cell size and viscosity of the surrounding solution, the manipulation force generated under a specific operating condition can be estimated from the terminal velocity of the cells. The terminal velocity is defined as the maximum dragging velocity of a moving lightbar that can manipulate the cells

III. The cell counts for the cell membrane lysis rate and nucleus separation rate calculation

	Test1	Test2	Test3
Total number of	96	87	116
cells			
Number of cells	84	69	88
expressing green			
fluorescence			
Total number of	66	81	100
cells expressing			
only green			
fluorescence			
Number of cells	52	68	72
expressing green			
fluorescence in the			
upward channel			

Supplemental Table S2: The sample sizes for the number of objects counted

IV. Finite-element-analysis (FEA) to numerically simulate the electric field

In order to know the actual voltage applied to the medium space, the cells therein and the electric field strength, we used finite-element-analysis (FEA) to numerically simulate the electric field. The conductivity of the medium was measured to be 3.4 μ S/cm. The conductivity of a-Si:H was measured to be 5×10⁻³ S/m. The voltage applied between two ITO layers was set as 28.5 Vpp. The simulated results are shown as follows.



Supplemental Figure S3 : Electric potential distribution in the medium.

As shown in this figure, the actual voltage applied in the medium could reach almost about 20 Vpp after light illumination. Besides, we could clearly observe the distribution of the electric potential in the medium space. Similarly, the electrical field was also numerically simulated. The maximum value of the electric field could reach $\sim 10^6$ V/m, which was an appropriate value to induce transmembrane potential for cell lysis in our study.



freq(18)=8500 Surface: Electric field norm (V/m)

Supplemental Figure S4 : Electric field distribution in the medium.

Moreover, we further calculated the transmembrane potential which is an important factor for cell lysis to prove that our developed system could achieve cell lysis sufficiently. The results show that our system could reach the critical transmembrane potential along cell membrane (1V).



Supplemental Figure S5 : Induced transmembrane potential distribution on cells.