Supplementary Information

Nanophotonic Cell Lysis and Polymerase Chain Reaction (PCR) with Gravity-Driven Cell Enrichment for Rapid Detection of Pathogens

Byungrae Cho^{†,‡,§}, Sang Hun Lee^{†,§}, Jihwan Song^{†,}, Saptati Bhattacharjee[†], Jeffrey Feng[†], SoonGweon Hong^{†,§}, Minsun Song^{†,‡,§}, Wonseok Kim^{†,§}, Jonghwan Lee^{†,§}, Doyeon Bang^{†,§}, Bowen Wang[†], Lee W. Riley[∥] and Luke P. Lee^{†,‡, §,⊥,#,¶,*}

[†] Department of Bioengineering, University of California Berkeley, CA 94720, USA

[‡]UC Berkeley and UCSF Joint Graduate Program in Bioengineering, Berkeley/San Francisco, USA

[§] Berkeley Sensor and Actuator Center, University of California Berkeley, CA 94720, USA

^{II}Division of Infectious Disease and Vaccinology, School of Public Health, University of California, Berkeley, CA 94720, USA

¹ Department of Electrical Engineering and Computer Science, University of California Berkeley, CA 94720, USA

[#] Biophysics Graduate Program, University of California Berkeley, CA 94720, USA

[¶] Biomedical Institute for Global Health Research and Technology (BIGHEART), Yong Loo Lin School of Medicine and Faculty of Engineering, National University of Singapore, Singapore 119077

Present Address: Department of mechanical engineering, Hanbat National University, Daejeon 34158, Korea.

*To whom correspondence should be addressed (E-mail: lplee@berkeley.edu)

This file contains:

Computational simulations of flow characteristics

Supplementary Figures 1-10.

Supplementary References 1-3.

COMPUTATIONAL SIMULATIONS OF FLOW CHARACTERISTICS

Numerical simulations were performed using commercial software (COMSOL Multiphysics 5.0; COMSOL, Inc.). To calculate laminar two-phase flow, phase field model that is appropriate to consider two-phase system was considered with the contributing forces. In addition, Navier-Stokes and continuity equations were considered, and the fluid flow was assumed to be laminar, steady, viscous and incompressible. The governing equations of phase field model based on the Cahn-Hilliard equation are employed as follows.

$$\frac{\partial \phi}{\partial t} + \mathbf{u} \cdot \nabla \phi = \nabla \cdot \frac{\gamma \lambda}{\varepsilon^2} \nabla \phi , \qquad (1)$$

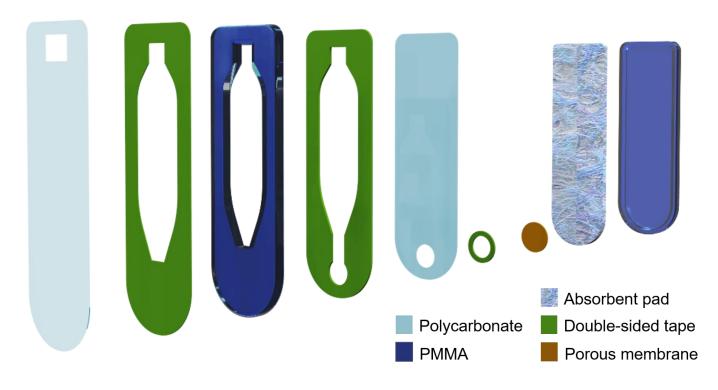
$$\varphi = -\nabla \cdot \varepsilon^2 \nabla \phi + (\phi^2 - 1)\phi, \qquad (2)$$

, where ϕ is the phase field function and it is defined as $\phi = 1.0$ in air and $\phi = 0.0$ in solution sample. **u**, γ , λ , ε are the fluid velocity, mobility, mixing energy density, and interface thickness, respectively. The surface tension is proportional to the ratio between the mixing energy density and the interface thickness as $F_s \propto \lambda/\varepsilon$. The fluid velocity is calculated with Navier-Stokes and continuity equations as follows.

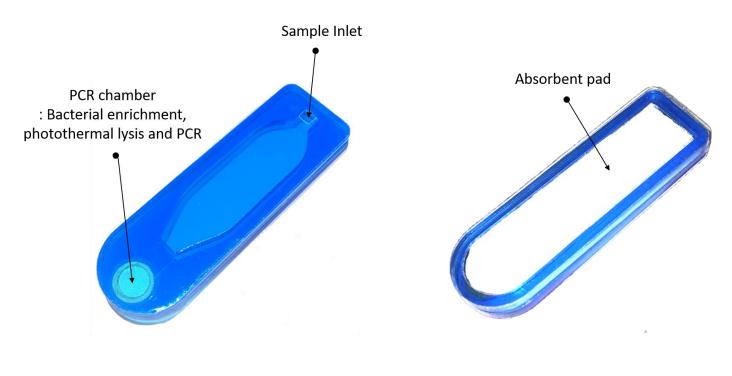
$$\rho \frac{\partial \mathbf{u}}{\partial t} + \rho(\mathbf{u} \cdot \nabla)\mathbf{u} = \nabla \cdot \left[-p\mathbf{I} + \mu(\nabla \mathbf{u} + (\nabla \mathbf{u})^T\right] + F_s + \rho \mathbf{g}$$
(3)

$$\nabla \cdot \mathbf{u} = 0 \tag{4}$$

, where ρ , μ , p and **g** represent the density of fluid, dynamic viscosity of fluid, pressure, gravity vector, respectively. F_s is the surface tension force. The fluid was considered to be water, and its density and dynamic viscosity were set as 10^3 kg/m^3 and 10^{-3} Pa/s. The thickness of interface was set to be $h_c/2$, where h_c is the characteristic mesh size in the region passed by the interface. The surface tension was set to be 0.07 N/m. The atmospheric pressure condition was assigned at the inlet. At the outlet, the five different outflow rates were assigned to describe the absorption by the pad. Wetted wall boundary conditions were applied at all device walls to describe the surface tension.



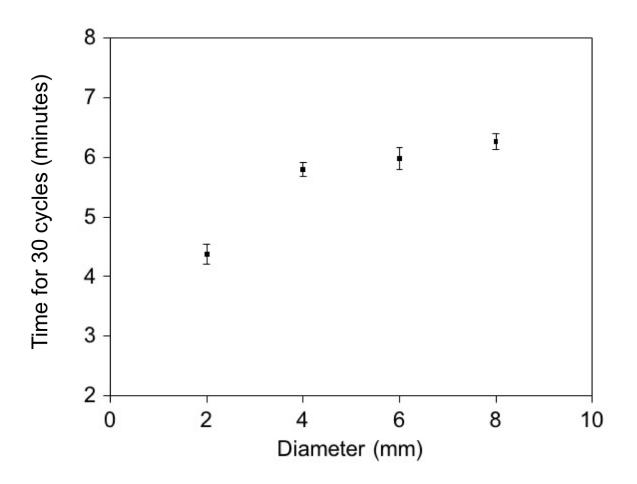
Supplementary Figure 1. The exploded of the LIGHT.



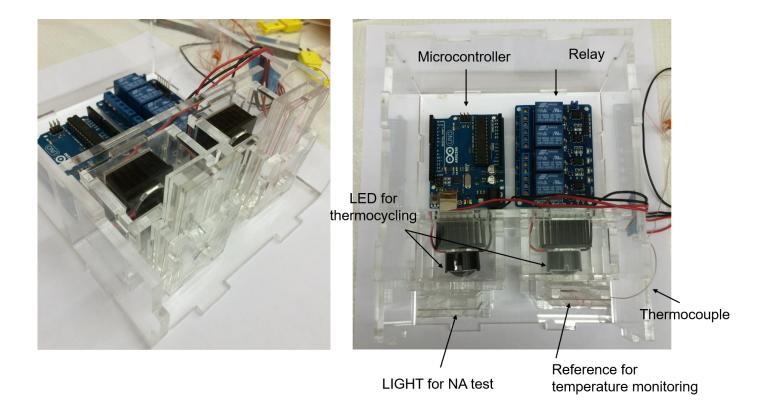
Front side

Back side

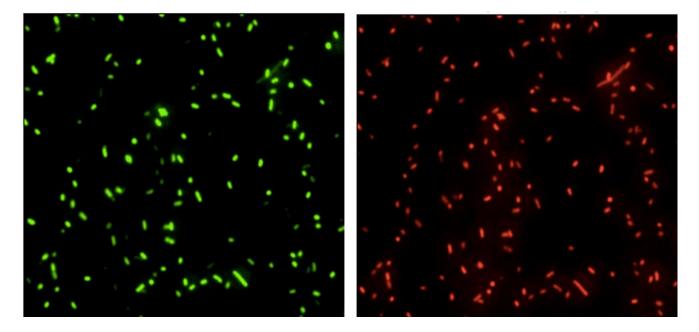
Supplementary Figure 2. Photograph of the LIGHT for rapid and precise identification of pathogens in urine samples.



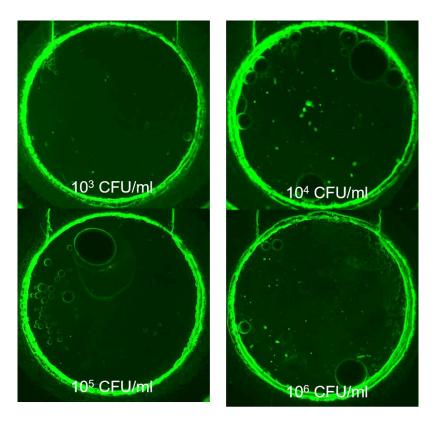
Supplementary Figure 3. Time for 30 PCR thermal cycles obtained with different diameters of the chamber.



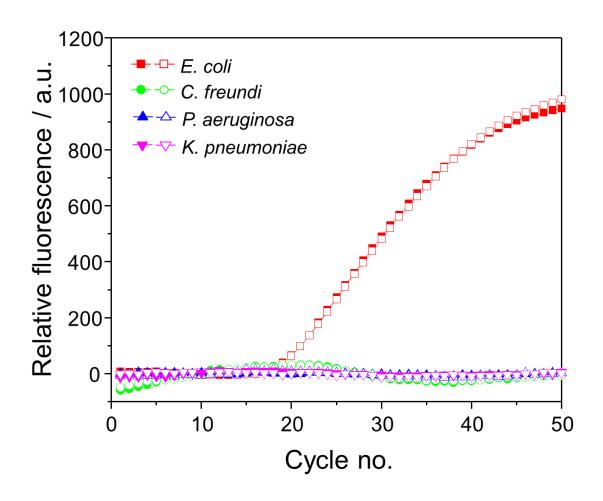
Supplementary Figure 4. Configuration of the LIGHT setup.



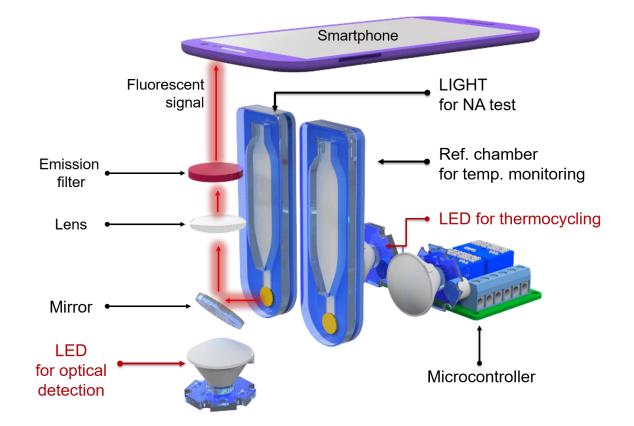
Supplementary Figure 5. Fluorescent images of *E. coli* after the illumination of a blue light ($\lambda = 447.5$ nm) for 1 minute. Green dye: all bacteria (SYTO 9 stain), Red dye: dead bacteria (propidium iodide stain).



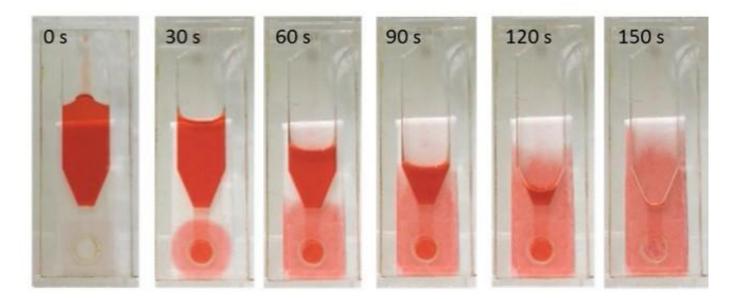
Supplementary Figure 6. Fluorescent detection of *E. coli* from 10^3 to 10^6 bacterial concentration.



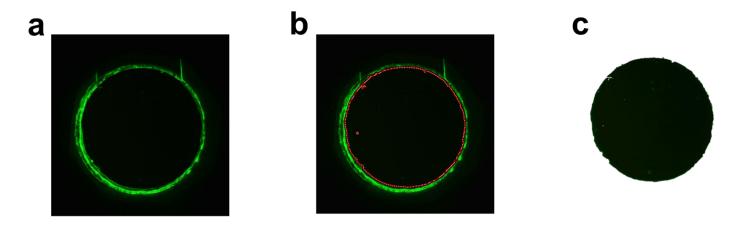
Supplementary Figure 7. The specificity of TaqMan probe for *E. coli*. Four types of bacteria strains including *E. coli*, *C. freundi*, *P. aeruginosa*, and *K. pneumoniae* at 10^5 CFU/ml were tested by using benchtop thermal cycler.



Supplementary Figure 8. Configuration of the LIGHT integrating optical detection module.



Supplementary Figure 9. Sequential images of bacterial enrichment in the LIGHT.



Supplementary Fig. 10. Representative fluorescent images: (a) The original image (b) The selected image by Magic wand tool in Photoshop (c) The extracted image.

Supplementary References

1. Qiu, X.; Ge, S.; Gao, P.; Li, K.; Yang, S.; Zhang, S.; Ye, X.; Xia., N.; Qian, S.; A Smartphone-Based Point-Of-Care Diagnosis of H1N1 with Microfluidic Convection PCR. *Microsyst. Technol.* **2017**, *23*, 2951-2956.

2. Angus, S. V.; Cho, S.; Harshmanb, D. K.; Song, J.-Y.; Yoon, J.-Y. A Portable, Shock-Proof, Surface-Heated Droplet PCR System for *Escherichia coli* Detection. *Biosens. Bioelectron.* **2015**, *15*, 360-368.

3. Gou, T.; Hu, J.; Wu, W.; Ding, X.; Zhou, S.; Fang, W.; Mu, Y. Smartphone-Based Mobile Digital PCR Device for DNA Quantitative Analysis with High Accuracy, *Biosens. Bioelectron.* **2018**, *120*, 144-152.