Supplementary Information

An integrated microwell array platform for cell lasing analysis

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Figure S1. Simulation of the scattered field of the incident Gaussian beam

(a) The simulation geometry. $n_{\text{water}}=1.33$. $n_{\text{mirror}}=1.45$. A Gaussian beam along y-axis is set as the background field with an FWHM of 60 $\mu$m and the focal plane at the top interface between the mirror and water. (b) The distribution of the scattered field when there is no microwell structure (the SU-8 domain is set to be the same as the water domain, $n_{\text{SU-8}}=1.33$). (c) The distribution of the scattered field when the microwell is present ($n_{\text{SU-8}}=1.60$). The integration of the scattered field energy density over the water domain is 2.45e-19 and 2.60e-19 J/m$^3$ without and with the SU-8 microwell structure, respectively. The discrepancy is less than 10%, thus we conclude that the microwell structure does not have any significant effect on the excitation profile.
Lasing stability of a cell captured in a microwell. The cell was continuously excited for 30 seconds with a pump intensity of 100 μJ/mm² per pulse. The cell underwent up to 600 excitation pulses during the test, about twice the number of pulses that a cell might receive when it was scanned for 6 times in our work. As shown in Figure S2, no wavelength shift is observed in those lasing peaks.
The thermal effect on the microwell-integrated cell lasing array

Given that there is environmental temperature fluctuation during the experiment, the resulting lasing wavelength shift is examined as follows. The dependence of the lasing wavelength $\lambda$ on temperature can be written as

$$\frac{\Delta \lambda}{\lambda} = \left( \frac{1}{n_{\text{eff}}} \frac{dn_{\text{eff}}}{dT} + \frac{1}{L} \frac{dL}{dT} \right) \Delta T,$$

where $n_{\text{eff}}$ is the effective refractive index, $d \lambda / dT$ the thermal-optic coefficient, $L$ the cavity length and $dL / dT$ the linear thermal expansion coefficient. A cell laser cavity consists of mainly water, DNAs and proteins, with an effective thermal-optic coefficient estimated to be $-1\sim4 \times 10^{-4}/\degree\text{C}$. Since the SU-8 layer acts as the spacer for the laser cavity, the linear thermal expansion coefficient of SU-8 ($52 \times 10^{-6}/\degree\text{C}$, MicroChem Corp.) is used to estimate $1/L dL / dT$. Thus, for a temperature drift of $1\degree\text{C}$, $|\Delta \lambda / \lambda| < 0.05\%$ and the corresponding lasing wavelength shift $\Delta \lambda$ around 540 nm is about 0.2 nm.

We also examine the thermal effect of the pump laser. At $120 \mu\text{J/mm}^2$ pump fluence, the total energy impinged on an area of $2 \times 10^{-4} \text{mm}^2$ (the area of a cell) is $2.4 \times 10^{-8} \text{ J}$ per excitation pulse. Typically, less than 10% of the total energy can be absorbed (absorption cross section of dyes at excitation wavelength $\sigma_a \sim 1 \times 10^{-16} \text{ cm}^2$, dye concentration $C \sim 1 \text{ mM}$, gain medium length $L \sim 10 \mu\text{m}$, thus absorbance $A = \sigma_a C L = 0.06$) and only a fraction that non-radiatively dissipates turns into heat (assume to be 40%, since quantum yield of SYTO9=0.6). The resulting fluctuation in local temperature is estimated to be around $0.3 \degree\text{C}$ ($\Delta T = E_{\text{heat}} / C_p m$, $E_{\text{heat}}$ the energy that turns into heat, $C_p$ the specific heat (water: $4.184 \text{ J/(g\cdot\degree\text{C})}$), $m$ the mass). The lasing wavelength might have a drift of 0.06 nm accordingly. However, no build-up effect is expected under continuous pulse excitation due to the small duty cycle (5 ns/50 ms) of the 20 Hz OPO laser.
References