Supplementary Information

Optofluidic lasers with a single molecular layer of gain

Qiushu Chen,^a Michael Ritt,^b Sivaraj Sivaramakrishnan,^{a,b} Yuze Sun^c and Xudong Fan^{*a}

^aDepartment of Biomedical Engineering, University of Michigan, Ann Arbor, MI 48109, USA

^bDepartment of Cell and Developmental Biology, University of Michigan, Ann Arbor, MI 48109, USA

^cDepartment of Electrical Engineering, University of Texas at Arlington, Arlington, TX 76019, USA

*xsfan@umich.edu

I. Theoretical analysis of a ring resonator laser with a single molecular layer of gain

Population inversion condition states that at the lasing threshold the round-trip emission should be equal to the sum of the round-trip cavity loss and the round-trip loss caused by molecular absorption.

Referring to Fig. S1, the cavity round-trip energy loss is determined by:

$$L_{cavity} = I \cdot \frac{2\pi m_1}{\lambda_0 Q_0} \cdot (2\pi R) = \left[\int \varepsilon_0 \varepsilon(r, \theta, z) E^2(r, \theta, z) r dr d\theta dz\right] \cdot \frac{2\pi m_1}{\lambda_0 Q_0} \cdot (2\pi R), \quad (S1)$$

where I is the total energy in the WGM. $\varepsilon(r,\theta,z)$ and $E(r,\theta,z)$ are the dielectric constant and WGM electric field. R and m_1 is the resonator radius and resonator effective refractive index, respectively. λ_0 is the lasing wavelength in vacuum. Q_0 is the resonator Q-factor. Assuming that the dielectric constant and the electric field have only radial dependence, Eq. (S1) becomes:

$$L_{cavity} = I \cdot \frac{2\pi m_1}{\lambda_0 Q_0} \cdot (2\pi R) = [2\pi \int \varepsilon_0 \varepsilon(r) E^2(r) r dr \cdot \int dz] \cdot \frac{2\pi m_1}{\lambda_0 Q_0} \cdot (2\pi R), \quad (S2)$$

The round-trip energy loss due to molecular absorption is given by:

$$L_{absorption} = 2\pi R \int \varepsilon_0 \varepsilon(r) E^2(r) \rho(r,\theta,z) \sigma_a(\lambda_0) r dr d\theta \cdot \int dz, \qquad (S3)$$

where $\rho(r,\theta,z)$ is the density of molecules. $\sigma_a(\lambda_0)$ is the molecule's absorption cross section at the lasing wavelength. For molecules attached to the resonator surface, we have

$$\rho(r,\theta,z) = A(\theta,z) \cdot \delta(R) = A\delta(R), \quad (S4)$$

where $A(\theta,z)$ is the molecular surface density. The dependence on θ and z can be removed if we assume a homogenous surface distribution. Similarly, the emission of the molecules can be given as:

$$Emission = 2\pi R \int \varepsilon_0 \varepsilon(r) E^2(r) \rho(r,\theta,z) \sigma_e(\lambda_0) r dr d\theta \cdot \int dz, \quad (S5)$$

where $\sigma_{e}(\lambda_{0})$ is the emission cross section at the lasing wavelength.

The corresponding population inversion condition for a four-energy-level laser system can be written as:¹⁻³

$$\eta(A_1/L)\sigma_e(\lambda_0) = \eta(A/L - A_1/L)\sigma_a(\lambda_0) + \frac{2\pi m_1}{\lambda_0 Q_0}, \quad (S6)$$

where A_1/L is the surface density of the molecules in the excited state normalized to the intensity decay length of the WGM in the liquid, which is the effective concentration of the molecules.

$$\eta = \frac{2\pi RL \cdot \varepsilon_0 (m_2 E_R)^2 \cdot \int dz}{2\pi \int \varepsilon_0 \varepsilon(r) E^2(r) r dr \cdot \int dz} = \frac{(m_2 E_R)^2 RL}{\int \varepsilon(r) E^2(r) r dr} \approx \frac{(m_2 E_R)^2 L}{\int \varepsilon(r) E^2(r) dr}, \quad (S7)$$



Figure S1. Illustration of the WGM and the parameters used in theoretical analysis.

where m_2 is the refractive index of the surrounding liquid. E_R is the WGM electric field at the ring resonator surface. η is the fraction of the WGM energy in the evanescent field.

According to the laser theory, the lasing threshold, I_{th}, is determined by:

$$I_{th} = \frac{\gamma}{\Gamma - \gamma}, \quad (S8)$$

where $\gamma = A_1/A$ is the fraction of gain molecules in the excited state at the lasing threshold. Γ is the fraction of gain molecules that participate in lasing action. Referring to Eq. (S6),

$$\gamma = \frac{\sigma_a(\lambda_0)}{\sigma_a(\lambda_0) + \sigma_e(\lambda_0)} (1 + \frac{2\pi m_1 L}{\lambda_0 \eta Q_0 \sigma_a(\lambda_0) A}) \approx \frac{2\pi m_1 L}{\lambda_0 \eta Q_0 \sigma_e(\lambda_0) A}.$$
 (S9)

II. Surface density ratio estimation for BSA specific binding and DNA hybridization

First we estimate the BSA surface density ratio between specific and non-specific cases. According to the laser theory, the laser output power, I_{output} , is linearly proportional to the pump intensity, I_{pump} , above threshold:

$$I_{output} \propto I_{pump} / I_{th} - 1.$$
(S10)

Since the output in Fig. 3(A) and (B) is nearly the same and the pump intensity is well above the respective threshold, based on Eqs. (S8) and (S10), 10 times difference in the pump intensity leads to:

$$\frac{I_{th,A}}{I_{th,B}} = \frac{\gamma_A}{1 - \gamma_A} \bigg/ \frac{\gamma_B}{1 - \gamma_B} = 0.1. \quad (S11)$$

Subscript A/B denotes the conditions in Fig. 3(A)/(B). Note that in Eq. (S11), we use Γ =1, since all the dye molecules on the surface participate in lasing action. Using γ_A =4.3% obtained by Eq. (S9) with m₁=1.45, $\lambda_0 = 520$ nm, $\eta Q_0 = 10^5$, $\sigma_e(\lambda_0) = 4 \times 10^{-16}$ cm², and A/L=170 µM, we arrive at $\gamma_A/\gamma_B = A_B/A_A = 0.14$, meaning that through specific binding processes the surface coverage of BSA is 14% of the non-specific case.

Using Eqs. (S8)-S(10) we can estimate the fraction of hybridized probe DNA cross-linked on the fiber surface based on the threshold difference. Referring to Fig. 4(D), after 10 nM target DNA incubation, Cy3 lasing threshold increases 3-fold. Thus,

$$\frac{I_{ih}}{I_{ih}} = \frac{\gamma'}{\Gamma' - \gamma'} / \frac{\gamma}{1 - \gamma} = 3, \qquad (S12)$$

where the superscript denotes to the conditions after hybridization. In this case, Γ' is no longer unity after hybridization, since a fraction of Cy3 molecules are completely quenched by Cy5 through FRET and do not participate in lasing action. $\gamma' = \gamma$, considering that the total number of Cy3 molecules on the surface and the cavity loss remain the same and that the Cy5 absorption is negligible. γ' is estimated to be 3.7% (using m₁=1.45, $\lambda_0 = 600$ nm, $\eta Q_0 = 10^5$, $\sigma_e(\lambda_0) = 4 \times 10^{-16}$ cm², and A/L=170 µM), which leads to $\Gamma' = 36\%$, meaning that 64% of the probe DNA is hybridized with the target DNA.

Probe DNA	5' - Biotin - AC AAC AAA GAA CAA ATA TAC ATA TAT GAT ATA ACA ACA AA -
Target DNA	5' - Cy5 - TT TGT TGT TAT ATC ATA TAT GTA TAT TTG TTC TTT GTT GT -3'

 Table S1. Modification and sequences of the 40 bases long single-stranded DNA.



Figure S2. Cy3-labeled probe DNA and Cy5-labeled target DNA are hybridized first and then cross-linked on the surface of the resonator. (Left panel) Control group. Probe DNA alone. Only Cy3 lasing is observed. (Middle panel) Hybridization ratio=2:1. Cy3 lasing is observed, but with a higher threshold and a lower emission efficiency. Cy5 lasing can also be observed, which verifies the presence of Cy5. (Right panel) Hybridization ratio=1:1. Cy3 lasing is completely suppressed. Stronger Cy5 lasing is observed, indicating more Cy5 molecules are on the resonator surface. In all three cases, the probe DNA concentration (and hence the Cy3 concentration) remains the same at 1 μ M. The excitation wavelength is 518 /625 nm for Cy3/Cy5 lasing.



Figure S3. (A) Ratio between laser emission from Cy3 in the presence and absence of the target DNA (Cy5) based on the solid curves in Fig. 4(D). (B) Ratio between fluorescence from Cy3 in the presence and absence of the target DNA (Cy5). Error bars are obtained with 5 measurements.

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- H.-J. Moon, Y.-T. Chough, and K. An, "Cylindrical Microcavity Laser Based on the Evanescent-Wave-Coupled Gain," Phys. Rev. Lett. 85, 3161-3164 (2000).
 Z. Li, and D. Psaltis, "Optofluidic dye lasers," Microfluid. Nanofluid. 4, 145–158 (2007).
 Y. Sun, and X. Fan, "Distinguishing DNA by Analog-to-Digital-like Conversion by Using Optofluidic Lasers," Angew. Chem. Int. Ed. 51, 1236-1239 (2012). 3.