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Optofluidic ring resonator laser with an edible liquid laser gain medium

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Abstract: We demonstrate a biocompatible optofluidic laser with an edible liquid laser gain medium, made of riboflavin dissolved in water. The proposed laser platform is based on a pulled-glass-capillary optofluidic ring resonator (OFRR) with a high Q-factor, resulting in a lasing threshold comparable to that of conventional organic dye lasers that are mostly harmful, despite the relatively low quantum yield of the riboflavin. The proposed biocompatible laser can be realized by not only a capillary OFRR, but also by an optical-fiber-based OFRR that offers improved mechanical stability, and is promising technology for application to *in vivo* bio-sensing.

OCIS codes: (140.0140) Lasers and laser optics; (140.2050) Dye lasers; (140.3948) Microcavity devices; (170.0170) Medical optics and biotechnology; (280.1415) Biological sensing and sensors.

References and links

1. D. Psaltis, S. R. Quake, and C. Yang, "Developing optofluidic technology through the fusion of microfluidics and optics," Nature **442**(7101), 381–386 (2006).
2. Z. Li and D. Psaltis, "Optofluidic dye lasers," Microfluid. Nanofluidics **4**(1-2), 145–158 (2008).
3. Y. Sun and X. Fan, "Distinguishing DNA by analog-to-digital-like conversion by using optofluidic lasers," Angew. Chem. Int. Ed. Engl. **51**(5), 1236–1239 (2012).
4. X. Fan and S. H. Yun, "The potential of optofluidic biolasers," Nat. Methods **11**(2), 141–147 (2014).
5. W. Lee, Q. Chen, X. Fan, and D. K. Yoon, "Digital DNA detection based on a compact optofluidic laser with ultra-low sample consumption," Lab Chip **16**(24), 4770–4776 (2016).
6. B. Helbo, A. Kristensen, and A. Menon, "A micro-cavity fluidic dye laser," J. Micromech. Microeng. **13**(2), 307–311 (2003).
7. T. W. Hansch, "Edible lasers and other delights of the 1970s," Opt. Photonics News **16**(2), 14–16 (2005).
8. C. Vannahme, F. Maier-Flaig, U. Lemmer, and A. Kristensen, "Single-mode biological distributed feedback laser," Lab Chip **13**(14), 2675–2678 (2013).
9. Y. Choi, H. Jeon, and S. Kim, "A fully biocompatible single-mode distributed feedback laser," Lab Chip **15**(3), 642–645 (2015).
10. M. C. Gather and S. H. Yun, "Single-cell biological lasers," Nat. Photonics **5**(7), 406–410 (2011).
11. Y.-C. Chen, Q. Chen, and X. Fan, "Lasing in blood," Optica **3**(8), 809 (2016).
12. S. Nizamoglu, M. C. Gather, and S. H. Yun, "All-biomaterial laser using vitamin and biopolymers," Adv. Mater. **25**(41), 5943–5947 (2013).
13. J. A. Rivera and J. G. Eden, "Flavin mononucleotide biomolecular laser: longitudinal mode structure, polarization, and temporal characteristics as probes of local chemical environment," Opt. Express **24**(10), 10858–10868 (2016).
14. H.-J. Moon, G.-W. Park, S.-B. Lee, K. An, and J.-H. Lee, "Laser oscillations of resonance modes in a thin gain-doped ring-type cylindrical microcavity," Opt. Commun. **235**(4-6), 401–407 (2004).
15. S. I. Shopova, H. Zhu, and X. Fan, "Optofluidic ring resonator based dye laser," Appl. Phys. Lett. **90**(22), 221101 (2007).
16. H. Chandrahalim, S. C. Rand, and X. Fan, "Fusion of renewable ring resonator lasers and ultrafast laser inscribed photonic waveguides," Sci. Rep. **6**(1), 32668 (2016).
17. C. Boehnke, U. Reuter, U. Flach, S. Schuh-Hofer, K. M. Einhäupl, and G. Arnold, "High-dose riboflavin treatment is efficacious in migraine prophylaxis: an open study in a tertiary care centre," Eur. J. Neurol. **11**(7), 475–477 (2004).

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18. F. Vollmer and S. Arnold, "Whispering-gallery-mode biosensing: label-free detection down to single molecules," Nat. Methods **5**(7), 591–596 (2008).

1. Introduction

Optofluidic lasers have been subject to intensive research over the last few decades, particularly for their potentials as bio-sensing platforms [1, 2]. Laser devices that utilize liquid gain media allow versatility in terms of optical analysis of biological analytes in aqueous condition that is common in nature, which was challenging for conventional solid-state lasers. Indeed, it was recently reported that a non-linearity of the lasing phenomena can lead to a digital-like sensing mechanism [3–5]. Since conventional bio-chemical sensors rely on fluorescence signals from target-bound fluorophores, which require precise and time-consuming analysis of the optical signals, the digital-like sensing paradigm can suggest the simple sensor platform, which is essential for the broad and general uses. The rapid, simple, and high-throughput optofluidic laser-based biosensor opens up many possibilities for *in vivo* bio-chemical analysis when integrated with, for example, endoscopy. However, a majority of the optofluidic lasers realized to date utilize organic dyes, such as Rhodamine, dissolved in their liquid laser gain media, most of which are toxic and non-biocompatible [2, 6]. The risk of a leakage of these non-biocompatible media restricts the laser devices from application to *in vivo* bio-systems.

Numerous efforts have been made since the early 1970s to realize an edible lasers with rhodamine- or fluorescein-dye-doped gelatin, which are not fatal when digested but still non-biocompatible [7]. Recent advances in biocompatible lasers have demonstrated the lasing phenomenon in riboflavin-doped gelatin and/or silk free standing films, enabling "fully biocompatible" laser light sources [8, 9]. However, in order to detect bio-analytes in their natural aqueous form with the laser as an active sensing mechanism, a biocompatible laser with liquid gain medium is essential. While bio-lasers with green fluorescent protein (GFP) or Indocyanine green (ICG) dye have been reported [10, 11], aqueous riboflavin and/or flavin mononucleotide (FMN) solution, which are abundant and widely found vitamin in nature and its derivative, were utilized as liquid laser gain media in recent studies [12, 13]. These riboflavin/FMN lasers have been realized with Fabry–Pérot (FP) microcavities and/or small droplets, which have difficulties in achieving superior lasing characteristics due to low Q-factors. Their relatively high lasing threshold as well as complexity of the microcavities fairly limits practical usefulness as the simple and rapid bio-sensing platform.

In this paper, we demonstrate an optofluidic laser device with an edible liquid gain medium in aqueous solution form. The laser utilizes a glass capillary optofluidic ring resonator (OFRR), and riboflavin dissolved in water as the liquid gain medium. The lasing threshold is estimated to be as low as 15.2 $\mu J/mm^2$, which is comparable to that of conventional optofluidic lasers with non-biocompatible organic dyes [6], such as rhodamine, owing to the extremely high Q-factor of the glass capillary OFRR [14, 15] that provides optical feedback for the lasing. This novel biocompatible laser can be realized by not only a capillary OFRR but also by the more mechanically reliable optical-fiber-based OFRR. Small footprint of the OFRR laser combined with recent advances in photonic waveguide inscription technique on a substrate [16], we can foresee potential integration of this laser with endoscopic systems, which can open up many possibilities for *in vivo* bio-chemical sensing/analysis.

2. Experimental

Riboflavin is a water-soluble B vitamin (vitamin B2) that is harmless even when excessive amounts are digested [17]. It is abundant in nature as well as in foods such as meat and dairy products, and is approved by the U.S. Food and Drug Administration (FDA) for both injection and dietary uses. Our proposed bio-compatible laser utilizes riboflavin dissolved in water as a laser gain medium. Since riboflavin has relatively low solubility in acidic water,

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the pH of the water for dissolving riboflavin is controlled to be 8.5, in order to meet normal drinking water conditions. When a concentration of 1 mM of riboflavin is dissolved in the pH-controlled water, the solution exhibits a bright yellowish-green color.

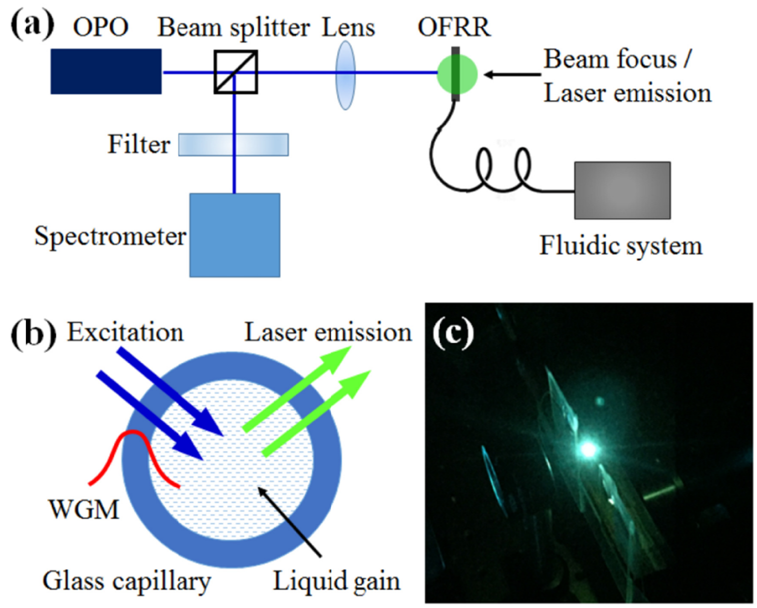

Fig. 1. (a) Schematic of the optical setup for measuring the laser emission from our OFRR laser with edible liquid gain medium. An external OPO pump light (wavelength = 485 nm) is focused on the glass capillary OFRR filled with riboflavin water solution through a confocal setup, and the laser emission is simultaneously collected by the spectrometer. The long pass filter (>500 nm) allows collection of only the laser emission from the riboflavin laser, without the scattered OPO pump light. (b) The glass capillary OFRR supports the whispering gallery mode (WGM) along its circumference, and the evanescent field of the confined light interacts with the liquid laser gain medium, providing feedback for lasing. (c) Photograph of the working OFRR laser.

An optofluidic ring resonator (OFRR) serves as the optical cavity of our proposed laser, which has several advantages over FP type or distributed feedback (DFB) lasers. The OFRR, which relies on total internal reflection, can easily realize an extremely high Q-factor, exceeding 10^6 [14, 15], and provides wavelength-independent optical feedback, which means that any edible liquid laser gain medium other than riboflavin can be used with the same configuration, while FP cavity with Bragg reflectors and DFB lasers require the design of optical structures tailored to the target wavelength.

We first infiltrate the aqueous riboflavin laser gain medium into a well-known pulled-glass-capillary OFRR [15, 18] with a home-built fluidic system as shown in Fig. 1(a). The glass capillary, with a diameter of 50 µm and a wall thickness of 3 µm, is filled with the edible liquid laser gain. The small dimension of the laser system is capable of potential integration to the endoscope and even intravenous injection needles (0.6 to 2.0 mm). A part of the OFRR (2 mm length) is subsequently pumped using an optical parametric oscillator (OPO) (Sourced by pulsed Nd:YAG laser, Spectra-physics, 6 ns pulse width, 10 Hz repetition rate) with a 485 nm wavelength. When the laser gain medium is externally pumped, light confined by the whispering gallery mode (WGM) supported by the OFRR evanescently interacts with the liquid laser gain medium filling out the hollow inside the glass capillary, providing optical feedback for lasing as illustrated in Fig. 1(b). The corresponding laser emission is simultaneously collected by a spectrometer (MonoRa 500i, Dongwoo Optron) through a confocal setup. Figure 1(c) shows a photograph of the lasing phenomenon, in which we can clearly observe the bright green laser emission scattered to free space. Even though riboflavin is known to have lower photo-stability compared to FMN [12], our OFRR laser is free of photo-bleaching owing to the circulating liquid laser gain through the fluidic channel.

3. Results and discussion

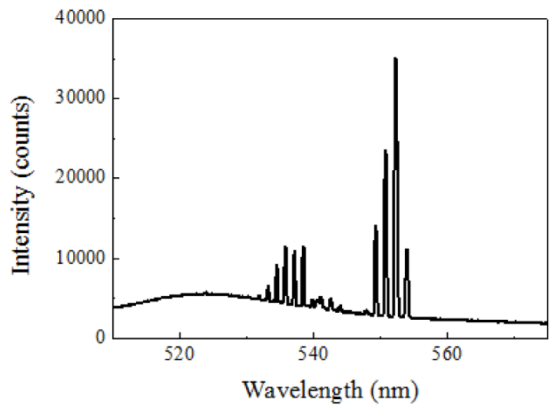

Fig. 2. Representative laser emission spectrum of our OFRR laser when the pump energy density is 96 μJ/mm^2. The spectrum exhibits the typical multi-mode lasing characteristic of the ring resonator laser with a free spectral range of 1.2 nm, which matches well with calculations made using the measured dimensions of the glass capillary OFRR.

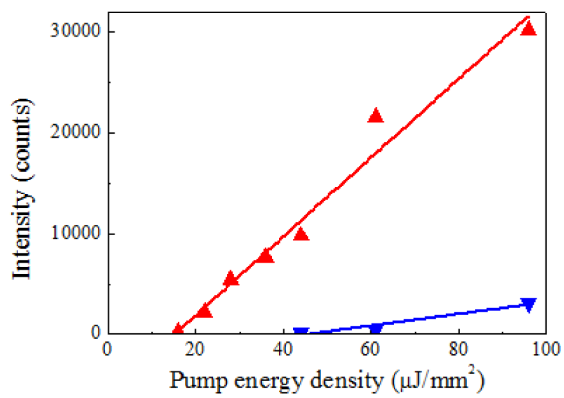

Fig. 3. Spectrally integrated laser emission intensities as a function of the pump energy densities. The red data set indicates when the concentration of riboflavin in water is 1 mM; the blue data set is for 0.5 mM concentration. The lasing thresholds of the two approximated from the linear fitting curves are 15.2 μJ/mm^2 and 46.3 μJ/mm^2, respectively. The lasing efficiency also shows a 7-fold decrease for the 0.5 mM laser. It is difficult to obtain laser emission when the riboflavin concentration is lower than 0.5 mM, even with excessively high pump energy density.

Figure 2 shows a representative laser emission spectrum for the proposed OFRR laser when it is pumped by the OPO at a pump energy density of 96 μJ/mm^2. The spectrum clearly exhibits the multi-mode laser characteristic that can be found in typical ring resonator lasers, and the laser emission is superimposed on a riboflavin fluorescence signal, which is due to the bulk riboflavin water solution that does not contribute to the lasing phenomena through the evanescent field. The diameter of the pulled glass capillary is measured to be around 50 μm; thus, the calculation of the free spectral range (FSR) given by an effective refractive index and the OFRR dimensions matches well with the observed FSR of 1.2 nm. This is a direct evidence that the OFRR filled with edible riboflavin laser gain medium successfully realizes the lasing phenomenon as intended.

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The spectrally integrated laser intensities as a function of the pump energy densities are illustrated in Fig. 3, in which the fluorescence background is rejected and integrated from 510

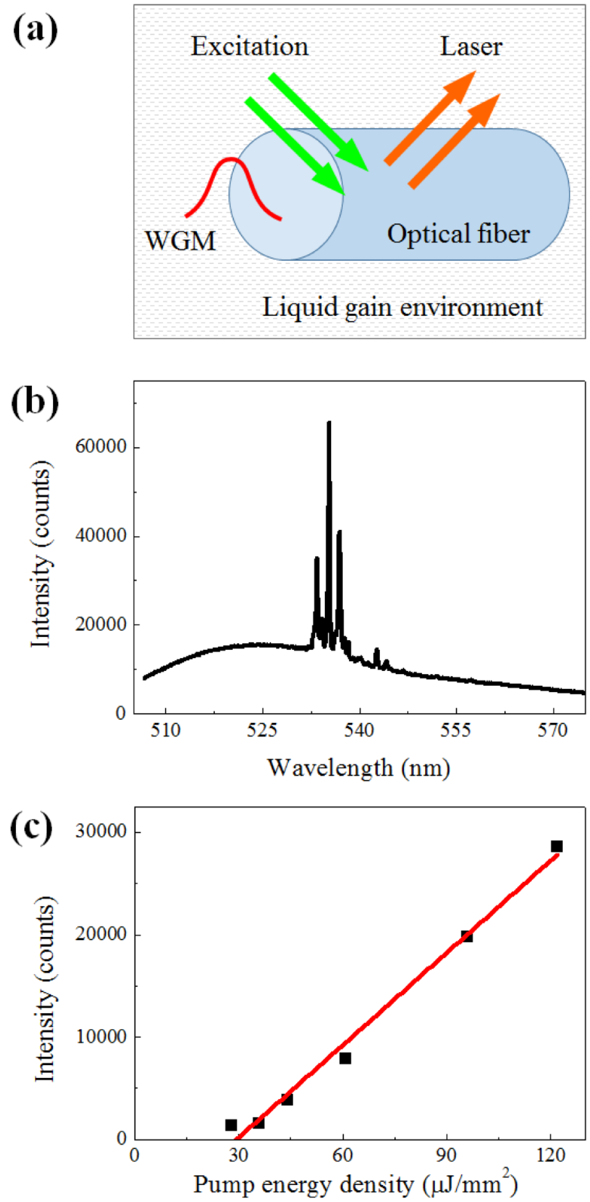

Fig. 4. (a) Schematic of the optical-fiber-based OFRR laser (b) Laser emission spectra when the pump energy density is 122 μJ/mm^2. (c) Spectrally integrated laser emission intensity as a function of the pump energy density. The lasing threshold is approximately 29.5 μJ/mm^2.

nm to 570 nm. The red data set indicates the laser intensities when the riboflavin concentration in the liquid gain medium is 1 mM, and a clear lasing characteristic with a lasing threshold of 15.2 μJ/mm^2 is observed. To study the concentration dependence of the lasing characteristics, the same configuration with a riboflavin concentration of 0.5 mM is measured, depicted by the blue data set. The lower concentration laser exhibits an increased lasing threshold at 46.3 μJ/mm^2, and the lasing efficiency also shows a 7-fold decrease. Laser emission cannot be obtained for a riboflavin concentration lower than 0.5 mM, even at

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excessively high pump energy density; thus, we conclude that 0.5 mM is the approximate minimum riboflavin concentration necessary to obtain laser phenomena in this configuration.

Our biocompatible laser can be realized not only by a pulled-glass-capillary OFRR, but also by various other optofluidic laser cavities with high Q-factors. Since the glass capillary has a wall thickness of only 3 µm, it has low mechanical stability, which limits the feasibility of its integration into endoscopic systems, even though the liquid laser gain medium is edible. Figure 4(a) illustrates the schematic for an optical-fiber-based OFRR. The polymer cladding of a commercial single mode optical fiber (SMF-28®, Corning®) with a 125 µm core diameter is removed, and the fiber is cleaned with acetone. The liquid chamber is produced with Polydimethylsiloxane (PDMS) and its 2 mm × 2 mm ×5 mm channel is filled with 1 mM riboflavin solution. The optical fiber OFRR is immersed in the liquid gain medium, and its 2 mm length part is subsequently pumped and analyzed using the same configuration as in Fig. 1(a). Light confined by the WGM and circulating along the circumference of the OFRR interacts with the surrounding liquid laser gain medium, and provides optical feedback for lasing via the evanescent field. Figure 4(b) depicts the laser emission spectrum when the pump energy density is 122 µJ/mm^2; very similar lasing characteristics to the capillary OFRR laser are observed. The FSR is reduced to 0.56 nm, which corresponds to the increased diameter of the OFRR, and matches well with theoretical expectations. The spectrally integrated laser intensities (as same as the data set in Fig. 3) for various pump energy densities are indicated in Fig. 4(c), and a clear lasing characteristic with a lasing threshold at 29.5 µJ/mm^2, similar to that of the capillary laser, is measured. It is thus shown that our biocompatible laser concept can be realized with the mechanically superior and easier to handle optical fiber OFRR. As mentioned earlier, recent advances in fabricating photonic waveguides on a glass/polymer substrate [16] opens possibilities of pumping / analyzing laser emission with waveguided lights, rather than free-space coupling, thus we can foresee potential integration of our biocompatible OFRR laser with small footprint into endoscopic systems/platforms for *in vivo* bio-sensing applications.

4. Summary

In this paper, we demonstrate an OFRR laser with an edible aqueous laser gain medium. The pulled-glass-capillary OFRR filled with riboflavin dissolved in water exhibits the typical multi-mode lasing emission spectrum of a ring resonator laser, as well as superior lasing characteristics with low lasing thresholds comparable to those of conventional organic dye lasers. This biocompatible laser is achievable with not only the capillary OFRR, but also with the optical fiber OFRR, which is easy to handle and free of risks of mechanical failure, assuming potential integration with endoscopic systems. Combining recent advances in biochemical sensing/analysis using bio-lasers, our proposed edible laser scheme can suggest a hint to open up novel *in vivo* bio-sensing systems in the near future.

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