Tailoring laser colors for super-multiplexed cell tagging

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The miniaturization of lasers has opened up a wide variety of new applications, including on-chip optical communications, laser displays, medical imaging, and sensing. A representative example is the cell laser that emerged in 2011, in which a single biological cell expressing green fluorescent protein generated laser emission under optical pumping with nanojoule pulse inside a Fabry–Pérot microcavity.[1] The ongoing miniaturization of lasers enables their incorporation into live cells, leading to the achievement of intracellular microlasers.[2] This significant progress has equipped individual cells with a distinctive coherent light source characterized by high brightness and sub-nanometer linewidth, paving the way for high-performance applications in microlaser-based cell sensing, tagging, and imaging.[3,4] For example, a remarkable achievement in massively multiplexed cell tagging was demonstrated by Seok-Hyun Yun and his coworkers in 2019, through the utilization of wavelength-encoded laser particles formed by semiconductor microdisks.[5]

Tailoring the emission wavelength of laser particles is the most important step for super-multiplexed cell tagging but is still very challenging. The emission wavelength of laser particles is mainly determined by varying their material compositions and particle sizes. In previous studies, the characteristic wavelengths of semiconductor microdisk laser particles were designed precisely with a deviation of 1 nm by patterning the microdisk with standard electron-beam lithography.[5–7] However, this technique faces challenges in generating laser particles of significant quantities, which is imperative for massively multiplexed cell tagging. Despite the fact that semiconductor microdisk lasers can be mass-produced by ultraviolet lithography, the low pattern precision in the microdisk diameter makes it difficult to design a unique color for each microdisk laser in one batch.[8] Now, reporting in *Advanced Photonics*, Seok-Hyun Yun and coworkers have developed a photo-electrochemical (PEC) etching method to tune precisely the lasing wavelength of laser particles with sub-nanometer accuracy after the ultraviolet lithography [Fig. 1(a)].[9]

The working principle of the wavelength tuning of laser particles through the PEC etching method is shown in Fig. 1(b). The PEC etching method depends on a light-induced electrochemical reaction, in which the pump light can design the reaction rate by varying the illumination power. This mechanism can be explained in the following three steps.

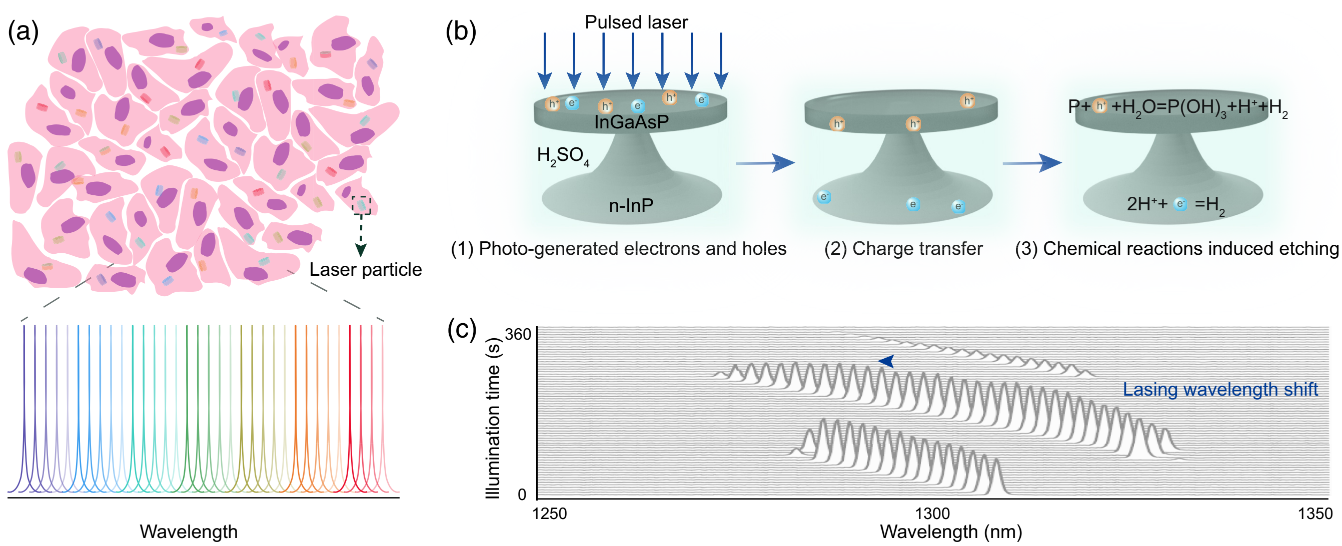

Fig. 1 Super-multiplexed cell tagging using laser particles with different colors. (a) Schematic of massively multiplexed cell tagging using laser particles, in which each cell is tagged by laser particles with different wavelengths. (b) The principle of the wavelength tuning of laser particles through PEC etching. A pulsed laser is used to illuminate the microdisk, which triggers not only the PEC etching but also the laser emission. (c) The gradual tuning of the characteristic wavelength of a single laser particle by PEC etching.

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1) The microdisk absorbs the photons of the pump light, generating electrons and holes.

2) The holes move to the InGaAsP microdisk surface while the electrons are driven to the surface of the n-InP substrate, due to the built-in potential between the semiconductor wafer and the sulfuric acid solution.[10]

3) The holes on the microdisk surface initiate the oxidation reaction whose oxide products are etched subsequently by acid solution. This decreases the microdisk diameter, which tunes the lasing wavelength.

To demonstrate the feasibility of this PEC etching method, Yun and colleagues first fabricated the microdisk lasers by the ultraviolet lithography on the semiconductor wafer, and then immersed the microdisks in a dilute sulfuric acid solution for the next-step PEC etching process. They used a pulsed laser to illuminate the microdisk, which triggered not only the PEC etching but also the laser emission. Therefore, the evolution of the lasing wavelength of the microdisk was monitored in real time during the PEC etching. Over illumination time, the lasing wavelength shows a rapid blue-shift and mode transition to a lower order, indicating continuous decrease of microdisk diameter [Fig. 1(c)].

To assess the wavelength tuning accuracy, for a 6×6 array of microdisks, each microdisk was tailored to a designed value in lasing wavelength under the real-time monitoring of the PEC etching. As a result, these microdisks showed an ultra-narrow distribution in lasing wavelength with a standard deviation of around 0.6 nm, which is one-order-of-magnitude narrower than that fabricated directly by the standard ultraviolet lithography. This allows sub-nanometer accuracy in the precise design of laser particle wavelengths. Additionally, Yun et al. transferred the laser particles into live cells for optical tagging, demonstrating that precise laser particles have the potential to track and monitor the functional viability of live cells.

This study by Yun's team presents a novel technology for PEC etching that enables precise control of the lasing wavelength of laser particles with sub-nanometer accuracy. The technology allows for real-time monitoring of the lasing wavelength during the PEC etching process, thereby eliminating the need for complex post-screening procedures. In the future, PEC etching could be utilized to customize the color of laser particles, thereby enhancing their multiplexing capacity in cell sensing, tagging, and imaging.

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Yun-Feng Xiao received his BS and PhD in physics from the University of Science and Technology of China in 2002 and 2007, respectively. After postdoctoral research at Washington University in St. Louis, he joined the faculty of Peking University in 2009, where he was promoted to tenured associate professor in 2014 and to full professor in 2019. His research interests lie in the fields of microcavity photonics, including quantum and nonlinear optics, asymmetric resonant cavities and wave chaos, and microcavity optical sensing. He is a fellow of Optica (formerly OSA) and has served on the organizing committee for more than 30 international conferences.