Electrostatic-responsive Microdroplet Lasers for Ultrasensitive Molecular Detection

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ABSTRACT

Electrostatics plays a critical function in most biomolecules, therefore monitoring subtle biomolecular bindings and dynamics via the electrostatic changes of biomolecules at biointerfaces has been an attractive topic recently and has provided the basis in diagnosis and biomedical science. Here we present a bioelectrostatic responsive microlaser based on liquid crystal (LC) droplet and explored its application for ultrasensitive detection of negatively charged biomolecules. Whispering gallery mode (WGM) lasing from positively charged LC microdroplets was applied as the optical resonator, where the lasing wavelength shift was employed as a sensing parameter. With the dual impacts from whispering-gallery mode and liquid crystal, molecular binding signals will be amplified in such LC droplet sensors. It is found that molecular electrostatic changes at the biointerface of droplet triggered wavelength shift in lasing spectra. The total wavelength shift increased proportionally with the adhering target concentrations. Compared to a conventional polarized optical microscope, significant improvements in sensitivity and dynamic range by four orders of magnitude were achieved. Our work indicated that the surface-to-volume ratio plays a critical role in the detection sensitivity in WGM laser-based microsensors. Finally, bovine serum albumin and specific biosensing using streptavidin and biotin were exploited to demonstrate the potential applications of microlasers with a detection limit on the order of 1 pM. We anticipate this approach will open new possibilities for the ultrasensitive label-free detection of charged biomolecules and molecular interactions by providing a lower detection limit than conventional methods.

Keywords: liquid crystal; whispering-gallery mode; droplet laser; biointerface; molecular sensing; electrostatic

INTRODUCTION

Molecular interactions provide the basis for detecting biomolecular binding events and dynamics. Electrostatics exhibits a critical effect on interactions of polar and charged molecules, such as proteins, nucleic acids, aqueous ions, and membrane lipids. Hence, developing an ultrasensitive and rapid detection method to monitor electrostatic changes of biomolecules at interfaces is of great significance.

Liquid crystals (LCs), with a wide variety of biological applications, are considered as a promising class of functional, responsive materials. Due to the interactions between LC molecules and biological targets, LC is high-sensitive to molecules anchoring and electrostatic force at interfaces. During the past several years, the LC biosensing platform has been explored in various forms, such as thin films[1-5] and microdroplets[6-12]. The orientation transition of LC molecules from homeotropic to planer (or from radial to bipolar) induced by biomolecules changing can be observed under a polarized optical microscope (POM) by the naked eye. However, to solve the difficulties in identifying the minor

variation of POM images, there are still many challenges. Recently, microlasers, as an emerging technology, attract widespread attention in the biomedical and biological fields. LC microsphere based whispering gallery mode (WGM) lasers, with the properties of high Q factor and compact cavities, have been demonstrated that it is a more sensitive method for biomolecules detection[7, 9, 13-15]. The dye-doped LC droplet, as a microcavity, can generate the WGM laser and is used to be a sensing probe as well. However, the detection limit of the WGM laser method still needs improvement.

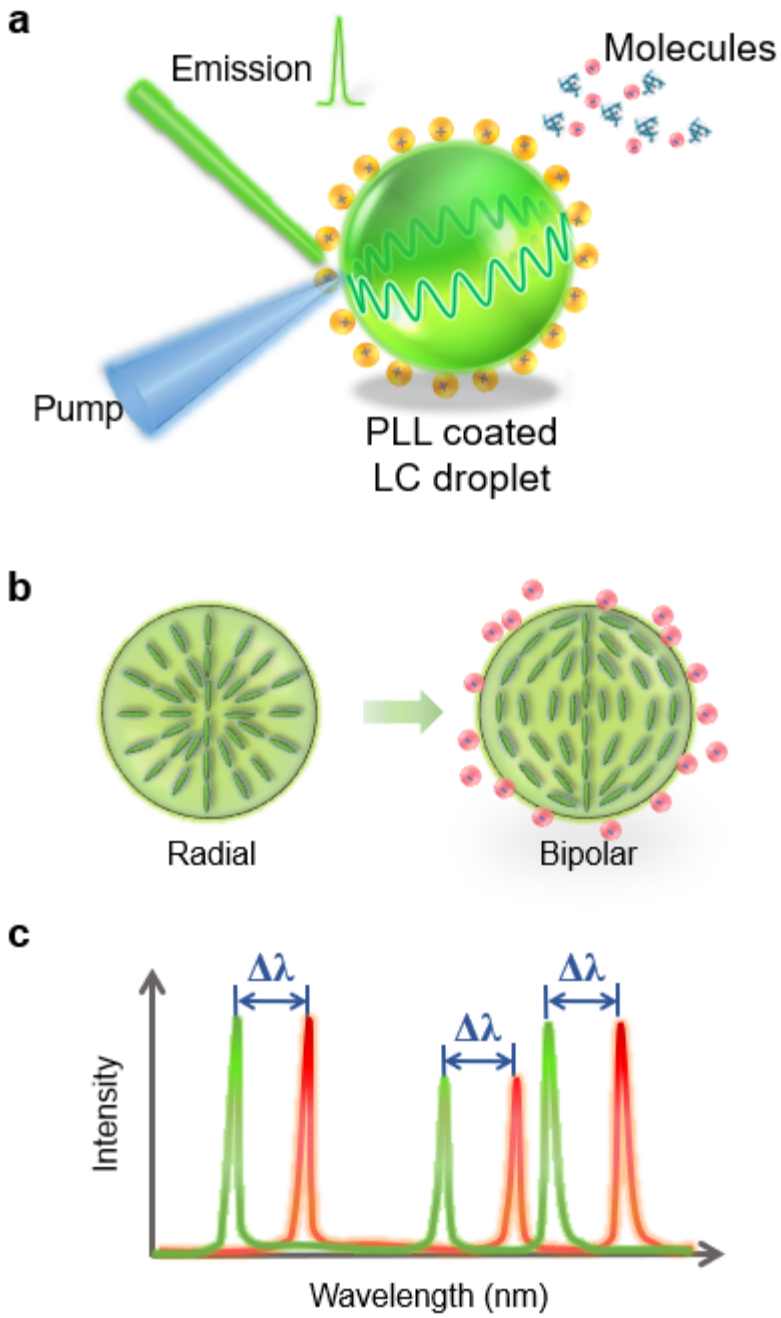

Figure 1. With the addition of negatively charged molecules, the illustration of (a) the experimental design, (b) orientation transition and (c) corresponding wavelength shift. Excitation wavelength = 478 nm.

In this work, based on WGM microlaser and positively coated LC droplets, we studied a novel and sensitive method to detect negatively charged biomolecules, as shown in Fig.1(a). The LC droplet is ultra-sensitive to electrostatic interaction was demonstrated by utilizing a negatively charged poly(4-styr-enesulfonic acid) (PSS) solution as an example. With the dual effect between WGM and LC molecules, the signal of target molecules variation will be amplified and lead to the wavelength shift in the lasing spectra increased as the concentration of biological targets increased. In addition, for biosensing, bovine serum albumin (BSA) was implemented, based on this electrostatic interaction at the LC interface. The detection limit of BSA molecules is 0.36 pM (2.4×10^{-11} g·ml^{-1}), and four orders of magnitude are significantly improved compared to the conventional POM methods. Our approach exhibits a clear conclusion that LC-based WGM lasing microsensors can be employed to monitor extremely low concentrations of label-free charged biomolecules and provide a potential tool for biomedical researches.

RESULTS AND DISCUSSION

We first revealed the possibility of achieving the responses of the WGM lasing spectra by electrostatic interaction at the interface of the coumarin 6 doped LC microdroplet. As such, poly-L-lysine (PLL) with positive charges was used to functionalize the surfaces of LC droplets and absorb the negatively charged biomolecules at the interface. With the attendance of targets, corresponding to electronics changes, the orientation transition of LC molecules from radial to bipolar and the wavelength shift of lasing spectra were induced, as shown in Fig.1(b). Therefore, the PSS solution for modifying the charges on the LC droplets interface was added to the solution, and a significant wavelength shift was presented in the lasing spectrum (Fig.1(c)). The interaction between PLL and PSS would lead to the reduction of the positive charges on the surface and the changes in the internal ordering of LC droplets. With the same droplet size (13 ± 0.5 μm), Fig.2 exhibits the responses of WGM lasing spectrum after adding various concentrations of PSS molecules (from 10^{-8} g·ml^{-1} to 10^{-3} g·ml^{-1}). Over the same time range (40 s), with the increase of PSS concentration, the spectral response of 5CB microdroplet is more significant. Moreover, our results also present a linear dependence of spectral shift on PSS concentrations, implying the surface charges are of great importance in the configuration of LC droplet. Therefore, WGM lasing spectra from LC droplets can be employed to monitor the electronegativity variation in the surroundings.

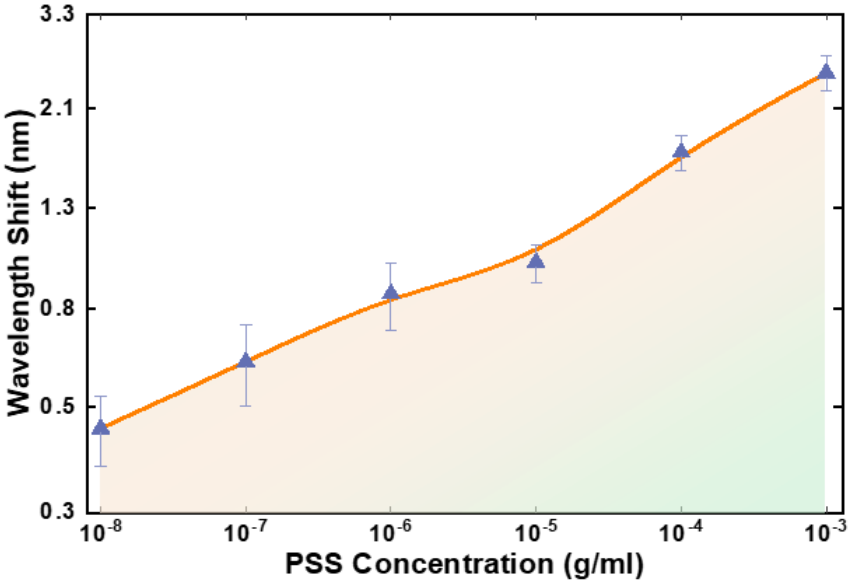

Figure 2. Comparison of the WGM lasing wavelength shift as a function of various PSS concentrations.

For further validation of biosensing possibility, as a target biomolecule, BSA was tested and variation of the LC droplets was observed. The spectral responses within 40 seconds are recorded and stable responsive data from the LC microdroplets can be obtained. The WGM lasing spectral responses under various concentrations of BSA (from 10^{-10}

g·ml^{-1} to 10^{-4} g·ml^{-1}) were also measured to verify the sensing ability of LC droplets. The wavelength shift of the spectrum against BSA concentrations in the logarithmic axis was plotted in Fig.3(a). A blue shift for 0.22 nm of the lasing spectrum from the LC droplet in 10^{-10} g·ml^{-1} BSA concentration could be observed. Under the high concentration (10^{-4} g·ml^{-1} BSA), the maximum detected wavelength shift is 5.45 nm. A linear dependence can be found, the limit of detection (LOD) based on this electrostatic interaction was calculated to be 2.4×10^{-11} g·ml^{-1} (0.36 pM). However, based on the method of POM images observation, only the BSA concentration above 10^{-7} g·ml^{-1}, the changes in LC can be distinguishable by the naked eye[16]. These results present the method of WGM lasing spectrum is four orders more sensitive than that of POM images in the detection of electrostatic interactions between biomolecules.

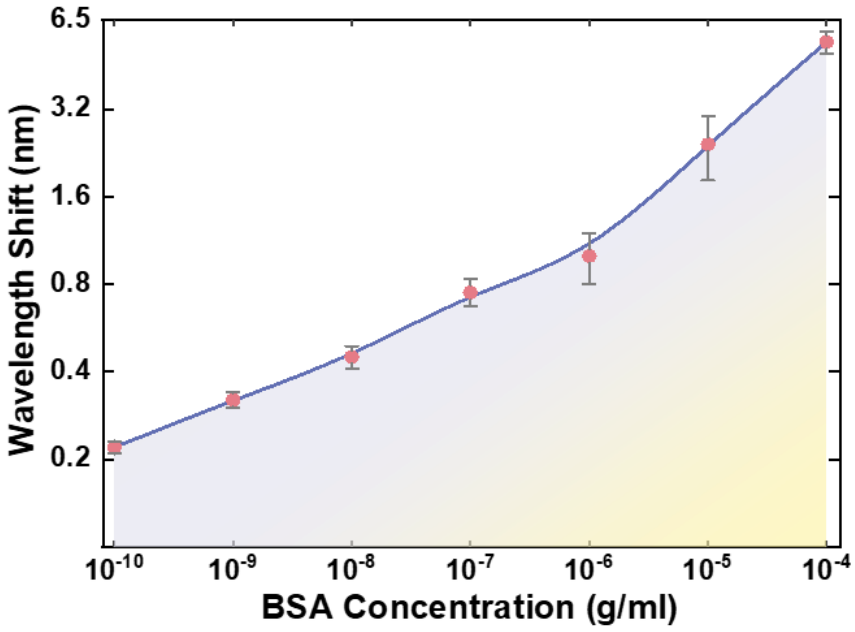

Figure 3. The lasing wavelength shift for the LC droplet with various concentrations of BSA.

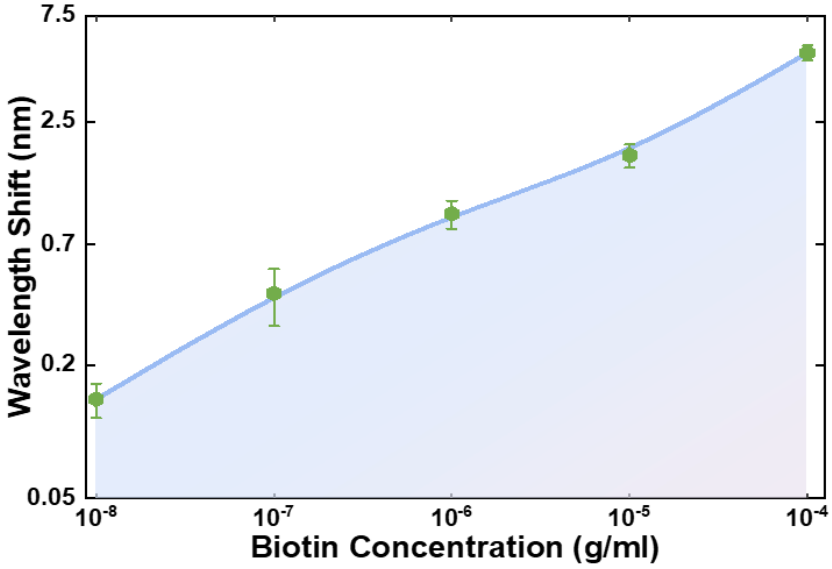

Figure 4. Summary of the lasing wavelength shift for the LC droplet with various concentrations of biotin.

In addition, streptavidin (SA) and biotin were employed to demonstrate the ability of LC droplets on specific detection. SA was coated on LC droplets, according to the specific binding events between SA and biotin, the wavelength responses proportionally increased with the biotin concentrations, seen in Fig.3(b). Therefore, LC WGM biolasers exhibit great potential in the sensitive detection of a wide range of biomolecules and electrostatic interaction at the surface.

CONCLUSIONS

In this work, we explored an electrostatic-sensitive LC droplet biolaser for biomolecules detection. The electrostatic interaction at the interfaces leading to the wavelength shift of the lasing spectrum from LC droplet was demonstrated. The wavelength shift increased linearly with the PSS concentrations. BSA, as an example of negatively charged biomolecules, was examined by LC droplet biolaser. Within 40 seconds, the wavelength shift increased proportionally with BSA concentrations and the detection limit is 0.36 pM. Compared to conventional POM images, four orders of magnitude were improved by the method of LC droplet biolasers. Moreover, the ability of specific detection of this LC biosensing platform was verified by employing SA and biotin. In conclusion, we envisage LC droplet biolaser, as a potential tool, can provide new possibilities for biomolecules detection.

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