

Microbubble-Assisted Preconcentration and Ultrasensitive Detection of Biomolecules Using Plasmonic Chiral Metamaterials

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Abstract: We demonstrate microbubble-assisted preconcentration of biomolecules on plasmonic moiré chiral metamaterials, enabling enantiodiscrimination of L-glucose and D-glucose at picomolar level, which is 10^7 times improvement in sensitivity. © 2020 The Author(s)
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1. Introduction

Plasmonic chiral metamaterials with strong chiroptical responses have proven to be promising in sensing biomedical chiral molecules such as amino acids, DNA and proteins [1]. However, despite recent advancements in plasmon-enhanced sensing of chiral molecules at picogram level [2], it remains challenging to enantiomerically detect chiral molecules below 1 mM, as required by practical applications in biomedical and pharmaceutical industries. Optically generated microbubble *via* plasmon-enhanced photothermal effects has recently emerged as an effective way to print and concentrate nanoscale particles and molecules on plasmonic substrates to further enhance the light-matter interactions for sensing [3,4]. Herein, using the microbubble-assisted concentration of molecules on moiré chiral metamaterials (MCMs), we demonstrate the ultrasensitive (~ 100 pM) label-free enantiodiscrimination of L-glucose and D-glucose. Our method shows 10^7 times greater sensitivity than the state-of-the-art chiral sensing techniques, paving the way for ultrasensitive enantioselective discrimination of chiral molecules in applications including biomarker detection and drug development.

2. Results and discussion

As shown in Fig. 1(a), both left-handed (LH) and right-handed (RH) MCMs consist of two layers of nanohole arrays with interlayer rotation. The optical chirality can be tuned by their interlayer rotation angle (Fig. 1(b)). The strong chiroptical effects of MCMs greatly enhance the interactions between circularly polarized light and adsorbed chiral molecules, enabling the detection of molecular chirality [5]. To improve the number of molecules adsorbed near the electromagnetic hot-spots of the metamaterial, a laser is applied to generate microbubble on the MCM to attract suspending molecules from the solvent toward the substrate *via* Marangoni convection (Fig. 1(c)). The simulated temperature distribution and flow velocity around the bubble are shown in Fig. 1(d) and (e). The microbubble-induced flow has a maximum velocity of ~ 800 mm/s, rapidly dragging molecules from hundreds of microns away towards the laser spot.

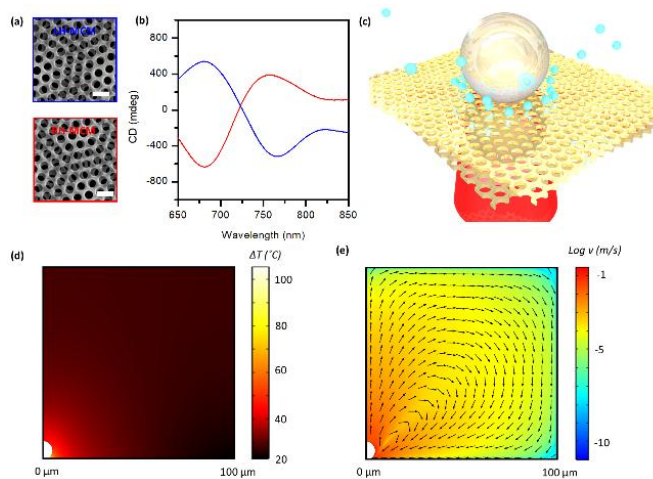


Fig. 1 (a) SEM images of the LH and RH MCMs, respectively. (b) CD spectra of the LH and RH MCMs. (c) Schematic illustration showing microbubble-assisted concentration of biomolecules on MCM. Simulated cross-sectional (d) temperature distribution and (e) flow velocity distribution around a laser-generated microbubble with diameter of 8 μm .

The enantiodiscrimination is achieved by comparing the CD spectra shifts of LH ($\Delta\lambda_{\text{LH-MCM}}$) and RH ($\Delta\lambda_{\text{RH-MCM}}$) MCMs after each bubble collapses. We have observed continuously opposite spectra shifts for D/L-glucose after multiple microbubble-assisted preconcentrations (Fig.2 (a,b)). We have further performed controlled experiments without microbubble-assisted preconcentration, in which the spectra shifts in the CD spectra of MCMs before and after the self-adsorption of D/L-glucose are characterized. The comparison in peak shifts demonstrates large enhancements in chiral sensing performances, as quantified by dissymmetry values ($\Delta\Delta\lambda = \Delta\lambda_{\text{LH-MCM}} - \Delta\lambda_{\text{RH-MCM}}$), induced by the microbubble preconcentration. As shown in Fig. 2 (c, d), when the molecular concentration decreases to below 10 mM, the dissymmetry values reduce to near zero for both D/L-glucose without microbubble-assisted preconcentration. When microbubble-assisted preconcentration is applied, the dissymmetry values are distinguishable down to 100 pM for both D- and L-glucose (corresponding to 18 pg/mL), showing 10^7 times greater sensitivity than the state-of-the-art chiral sensing techniques.

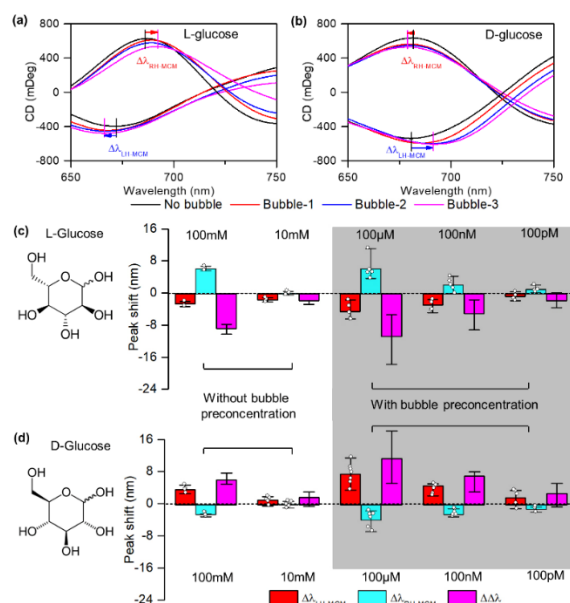


Fig. 2 (a,b) CD spectra of LH and RH MCMs after multiple microbubble-assisted preconcentration of D/L-glucose. (c, d) CD spectra shifts ($\Delta\lambda$) and dissymmetry values ($\Delta\Delta\lambda$) of (c) L-glucose and (d) D-glucose with and without microbubble-assisted preconcentration.

3. Conclusion

We demonstrate enantiodiscrimination of L-glucose and D-glucose at ultralow concentration (~ 100 pM) using the microbubble-assisted preconcentration of molecules on MCMs. With the rapid and ultrasensitive sensing performances, our method is promising for a wide range of applications in pharmacology and toxicology.

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