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

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***Abstract*—We achieve the ultrasensitive chiral detection of metabolites at picomolar level. The ultra-high sensitivity is enabled by microbubble-assisted accumulation of chiral molecules at the electromagnetic hot-spots of plasmonic chiral metamaterials, which could potentially provide first-line screening to identify diabetes case.**

Keywords— Metamaterials, microbubble, chirality, diabetes

I. Introduction

Plasmonic chiral metamaterials with strong chiroptical responses have proven to be promising in life science applications [1]. Recent advancements of chiral plasmonics have allowed the zeptomole detection limit of adsorbed molecules [2]. However, it still remains challenging to achieve detection below 1mM, limiting its practical applications. The optically generated microbubbles via plasmon-enhanced photothermal effects can print and concentrate nanomaterials on arbitrary substrates [3,4]. Herein, using the microbubble-assisted concentration of biomarkers on moiré chiral metamaterials (MCMs), we have achieved the enantiomeric discrimination of the chiral biomarker (i.e. glucose) with concentration down to 100 pM. The strongly enhanced sensitivity further enables the determination of enantiomeric excess of racemic solution of D/L-glucose with various ratios. Finally, as an example of clinical potentials, we apply this technique and detect the chirality of clinical mice/human urine samples induced by metabolite biomarkers (i.e. lactate acids) with ultra-small optical rotation. Our results show that diabetic human urines are more dextrorotatory than normal human urines, which may benefit future chirality-related detection of diabetes.

II. Results and discussion

Our MCMs consist of two layers of nanohole arrays with specific interlayer rotation angle. The optical chirality can be tuned by their interlayer rotation angle (Fig. 1(a)). Our group has previously demonstrated the enantiomeric discrimination of a chiral drug molecule (R-thalidomide) and its toxic enantiomer (S-thalidomide) with trace amount of ~250 picograms [5]. However, due to the short decay length (nanometer scale) of the plasmonic field, the analytes should be either physically adsorbed on the surfaces or resided near the substrate. To overcome these limitations, we apply micro-bubble generated on the MCM to drag the biomolecule toward the substrate via Marangoni convection (Fig. 1(c)). As shown in Fig. 1 (d), the resultant flow velocity profile can be up to ~800 mm/s, which is much stronger than conventional preconcentration methods such as thermoelectric [6], thermophoretic [7] and electrothermoplasmonics [8].

We compared the CD spectra shift before and after each bubble collapses to identify molecular chirality. For the L-glucose, we observed a continuous redshift of CD spectra peak for RH-MCMs while a continuous blueshift of the CD spectra dips for LH-MCMs (Fig. 2a). For the D-glucose, it shows the opposite spectra shift indicating its opposite enantiomer to the L-glucose (Fig. 2b). We further applied this technique to detect the diabetic induced abnormal chirality of metabolites in urine. As shown in

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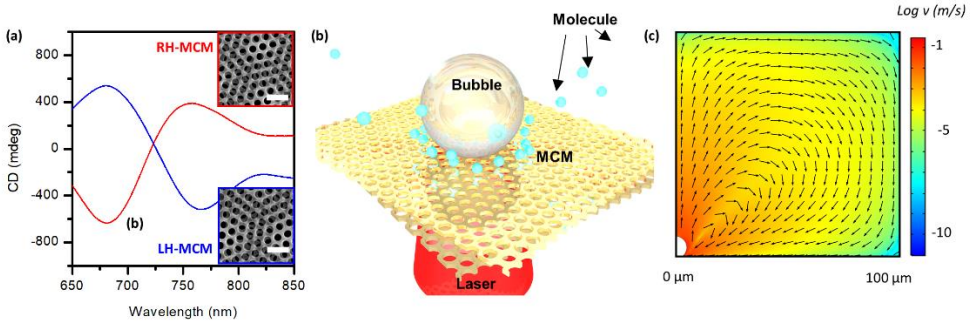

Fig. 1 (a) SEM images of the LH and RH MCMs, respectively. (b) CD spectra of the LH and RH MCMs. (c) Schematic illustration showing microbubble-assisted concentration of Biomolecules on MCM. (d) Simulated temperature distribution around an 8 µm bubble in a cross-sectional view. (e) Simulated flow velocity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

Fig. 2c, the average $\Delta\Delta\lambda/\lambda_{sum}$ ($\Delta\Delta\lambda = \Delta\lambda_L - \Delta\lambda_R$, $\lambda_{sum} = \Delta\lambda_L + \Delta\lambda_R$), where $\Delta\lambda_L$ is the CD spectral peak shift of LH-MCMs and $\Delta\lambda_R$ is the CD spectral dip shift of RH-MCMs, shows more positive value in diabetes human urine than the mice urine implying abnormal dextrorotary chirality of metabolites in diabetes human urine. By measuring D-glucose in healthy control and diabetes human urine, we showed that elevated D-glucose increase in urine contributes to the more dextrorotary in diabetes human urine.

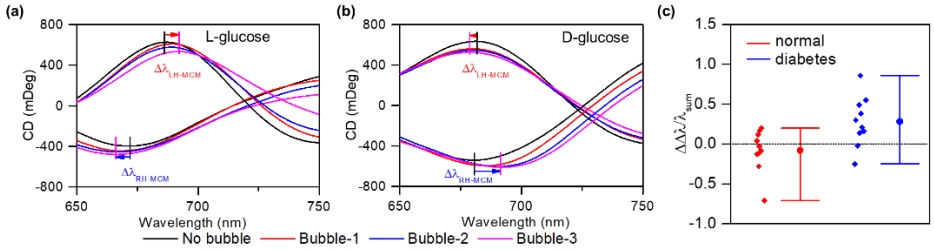

Fig. 2 (a,b) CD spectra of LH and RH MCMs for D/L glucose enantiodiscrimination after multiple microbubble-assisted concentration. (c) Dissymmetry value over the sum of the CD spectra shift ($\Delta\Delta\lambda/\lambda$sum) measured in diabetes and normal human urines.

III. Conclusion

We have developed rapid microbubble-assisted concentration and ultrahigh-sensitive detection of chiral metabolites. With their rapid and ultrasensitive detection, this method can be a critical candidate for a wide range of applications in rapid diabetic detection.

IV. Acknowledgment

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V. References

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