Microbubble-assisted concentration and ultrasensitive detection of chiral biomolecules using plasmonic chiral metamaterials

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Abstract

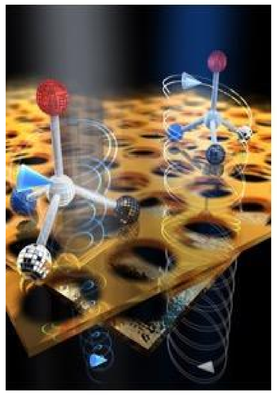
- Chiral molecule, the building blocks of human life, plays a key role in pharmaceutical and clinical industry because most enantiomers of chiral drugs have huge differences in biological activities including metabolism, toxicology, and pharmacology.
- Traditional methods including chiroptical spectroscopy, high-performance liquid chromatography, and X-ray crystallography are suffering from the large sample consumption, predesigned intermediate precursor, and time-consuming data processing.
- We developed new type of chiral sensor device based on plasmonic metamaterials called moiré chiral metamaterials (MCMs) with strong chiroptical response.
- Our proposed chiroptical nano-device can solve the unmet requirements in the pharmaceutical industry by providing enantiodiscriminative characterization of chiral molecules with low sample consumption, high sensitivity (i.e. low sample concentration), easy preparation and rapid processing.

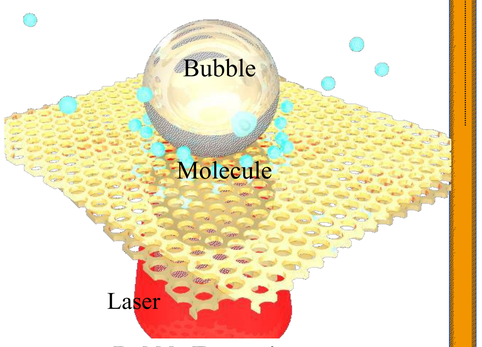
Comparison of Differentiation Parameters

DIFFERENTIATION PARAMETERS	Chiroptical Nano-Device	Chiroptical Spectroscopy	Liquid Chromatography	Crystallography
Sample Consumption	Low (1 – 10 μL)	High (~ 2mL)	Low (1 – 10 μL)	Medium (> 100μL)
Sample Concentration	Low < 1 μM	High (~ 10 mM)	Medium (~ 1 mM)	High (Solid)
Preparation	Easy dissolution	Easy dissolution	Tedious column development	Tedious crystallization process
Process Time	Short (< 1 day)	Medium (~ 1 day)	Long (~ 1 week)	Long (Several days)

Proposed Chiroptical Nano-device

- Strong interactions between chiral molecules and circularly polarized light enhanced by moiré chiral metamaterials.
- Lab-on-a chip microfluidic devices

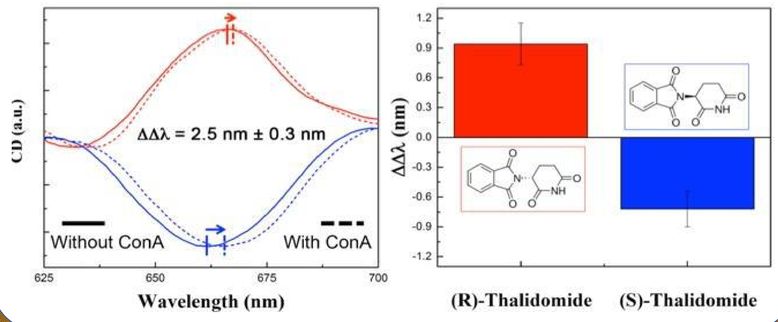




Bubble Formation

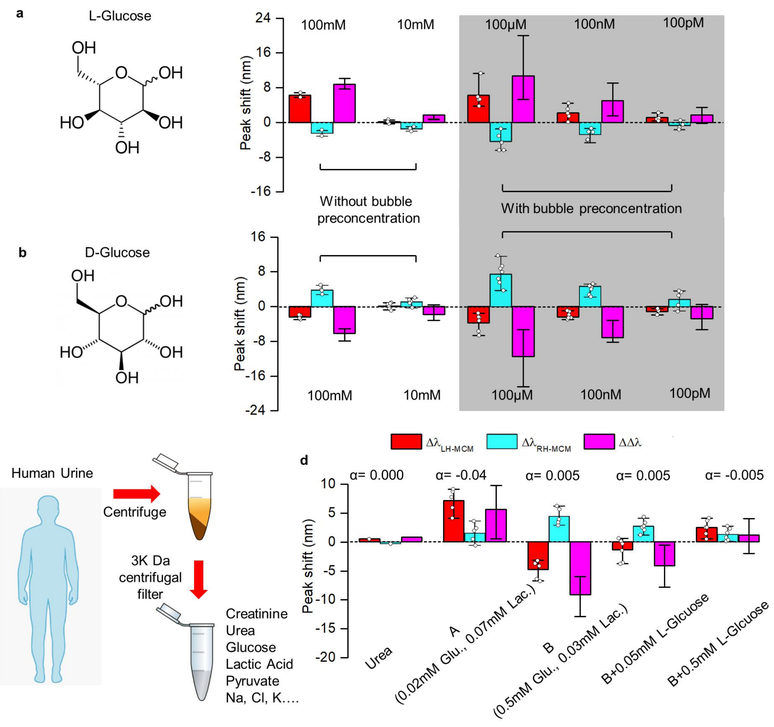
Detection of the Structural Chirality of Molecules using MCMs

- The adsorption of chiral proteins caused asymmetric spectral shifts of measured circular dichroism (CD) for the MCMs with opposite handedness (i.e. $\Delta\Delta\lambda=\Delta\lambda_{RH}-\Delta\lambda_{LH}$ is non-zero).
- We can also detect R-thalidomide and its "evil twin" at the picogram level.



Rapid Label-Free Profiling of Chiral Metabolite Biomarkers

- Microbubble-assisted concentration of analytes enables the label-free enantiodiscrimination of biomolecules at picomolar level, which is ~10^7 enhancement in comparison with state-of-the-art sensitivity
- Rapid diagnosis of diabetes.



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