Analytical Instrumentation, Methods & Materials

Volume-Free Reagent Addition and Exclusion-Based Sample Preparation Enables Multistep Microscale Assays

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The Wisconsin Alumni Research Foundation is seeking commercial partners interested in developing a liquid handling platform that allows microscale samples to be manipulated while addressing the sample loss, dilution and residual solvent challenges of microscale manipulations. This technology enables higher efficiency extraction of methylated DNA with potential for single-cell applications and has also been applied to microscale drug testing of antimicrobial agents. The technology can be extended to complex multistage sample manipulations to enable diverse applications.

Overview

Liquid handling is a critical step in biological assays and typically includes either a reagent addition or solution exchange process. However, it's challenging to manipulate samples on the microscale. Adding reagents can significantly dilute the sample and solution exchange might not be effective because of substantial residual solution. Additionally, manipulating microscale samples can lead to sample loss due to surface adsorption. Many of these challenges are not noticeable when larger volumes are used. Robust technologies for manipulating microscale samples would enable preparation of material-limited samples, allowing studies on rare samples or those in unique biological contexts, such as single-cell or low cell count samples.

The Invention

UW-Madison researchers have developed innovative strategies that allow researchers to manipulate microscale samples while avoiding key problems with handling microscale liquids, including sample loss during manipulations, dilution upon reagent addition and residual solution during solution exchanges. Their solution directly addresses some major challenges of microscale manipulation and is extendable to complex multistage sample manipulations.

First, aqueous droplets with magnetic beads are manipulated under oil on a solid surface, enabling near complete sample recovery by taking advantage of exclusive liquid repellency, whereby the aqueous droplet is fully repelled from the hydrophobic surface. Patterns of hydrophilic spots on the surface permit reliable and flexible manipulation across the surface.

Volume-free reagent addition is accomplished by manipulating the droplets over dried reagent spots and reconstituting reagents into the droplet without dilution. Analytes attached to magnetic beads can be rapidly and gently washed and exchanged into new solutions by transferring magnetic beads to new aqueous droplets under the oil. The use of dissolvable 'smart' valves allows controlled reagent delivery in this system. The aqueous droplets exhibit remarkable stability and are robust to plate titling and vigorous shaking without sample loss.

Applications

- High sensitivity extraction of methylated DNA for rare and valuable samples

- High-yield chromatin immunoprecipitation enabled by high recovery microscale manipulations with potential for single-cell applications
- Microscale drug testing

Key Benefits

- Enables analysis of low abundance molecules not previously accessible, with potential to scale to single-cell extractions
- Flexible technology allows extension to many multistage sample manipulation processes.

Stage of Development

Microscale drug testing has been demonstrated for antimicrobial susceptibility experiments using live cells.

Additional Information

For More Information About the Inventors

- David Beebe
- Joshua Lang

Publications

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Tech Fields

- Analytical Instrumentation, Methods & Materials : Microfluidics

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