Novel Fluidics Microreactor/Flow Cell Enhances Speed/Sensitivity of Bead-Based Bioassays 5-Fold
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Abstract
Automated purification and concentration of cells, nucleic acid, and proteins is critical to enable these detection in environmental, clinical and food samples. Automated magnetic reagent protocols allow for streamlined operations and can actually improve laboratory performance relative to assays conducted in a manual mode. The Pacific Northwest National Laboratory (PNNL) has developed a variety of devices and methods for automating sample preparation and detection. At the heart of these devices is a unique magnetic particle trap (Pacific Northwest National Laboratory) that allows surface functionalized magnetic or non-magnetic particles to be trapped with subsequent perfusion of analytes, reagents and wash solutions. This approach achieves rapid, parallel and scalable manual or robotic processing which can be configured to conduct automated or semi-automated workflows. We present the advantages of using bead-based workflows to analyze DNA and proteins, while significantly reducing sample waste effects.

Results are presented that highlight the analytical performance improvements obtained for automated microreactor assays using PNNL’s inhouse magnetic bead reagents capable of 1-10 fold higher “within-run” (i.e., in labs with robotized processing)

Introduction
Challenges for Detection in Complex Samples
• Variable background
• Background interferes with detection
• Problems with accuracy
• Traditional sensor approaches have limited system lifetimes
• Small amounts of pathogens can cause illness:
  Example: 1 pathogen/ml: 1.7 ml (1.7 x 10^16-20)
  - 1800 analyses per pathogen: 1.7 ml (1.7 x 10^19)

Need Purification AND Concentration
Automated Purification and Concentration of Cells, Biomolecules, and Chemicals

Functionalized Microbeads Enable Purification and Concentration
- Beads automatically delivered and released
- 100 nm nanomagnetic particles with magnetic cores is highly specific and of excellent quality
- Can reversibly bind, release, or needed for automation
- Enables novel, parallel and scalable workflows in an automated "media" robotic process
- Beads with polymeric ligands able to "grab" small molecules, larger molecules

Microreactor/Flow Cell Advantages
- Enhanced Mass Transport
- Lower Limits of Detection for Assays
- Faster reactions (seconds/minute)
- Efficient/Complete Washing
- Rapidly Removes interference in the system
- Microreactor/Flow Cell Advantages
- Microbeads Automatically Delivered/Released
- Microreactor/Flow Cell are Pre-Made for Disposable Cartridges
- Up to 12 Sample Parallel Processing
Design Adaptable to 96-Well Microplates

Electromagnetic Micro bead Trap
- Electromagnetic micro bead trap: magnetic particles are attracted to the trap
- Micrometer-sized bead trap allows for rapid separation of particles
- Analyte DNA isolated with the micro bead trap

Reproducible detection of 10 cells/ml, in river water concentrate
Without sample prep: PCR was inhibited, resulting in false negatives

Magnetic Micro bead Trap Allows Complete and Rapid Removal of PCR Inhibitors
- FBS-Free Barren Surface
- FBS-free protein resin matrix
- 10 Picomolar Protein Detection in 15 minutes

Summary
- Microreactor trap handles magnetic and non-magnetic microparticles of various shapes, sizes, material type
- Flow through design well-suited to automated platforms
- Reusable or disposable design
- Single channel, multi-channel (up to 10), or 96-well plate compatible
- Suitable to perform nanofluidic to larger volumes
- Provides sample concentration and purification
- Microfluidic platforms
- Surface magnetic bead functionalization for analysis of different organisms, bacteria, chemicals
- Including interferons
- Include only modules needed for particular application (e.g., cell capture)
- Can real-time multivariate detection types (integrates or downstream measurement)

Microreactor/Flow Cell improves sensitivity, speed, throughput

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