PATENT NO. US20210302300A1

LICENSING OPPORTUNITY: SERIAL CYTOMETRY

DESCRIPTION

Problem

It solves a significant problem in basic and clinical medical research of making precise measurements of objects in flow like characterizing a sample containing fluorescently labeled cancer cells.

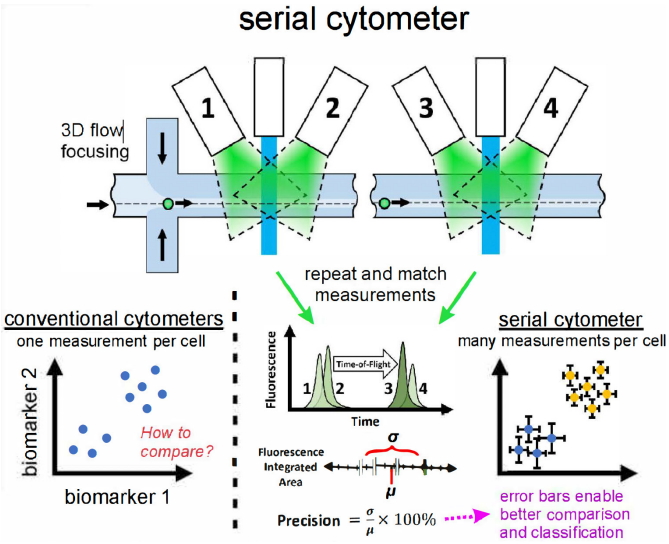
Invention

NIST scientists have developed a microfluidic flow cytometer that is capable of robust and repeated measurements that provide first-of-their-kind uncertainty estimates, which support better comparability and classification of cytometry data. The device measures single objects in flow several times along a microchannel with integrated waveguides that deliver and collect emitted, transmitted, and scattered light and provide additional details about object shape.

BENEFITS

Potential Commercial Applications

- Only cytometer capable of per-object uncertainties
- Better counting accuracy and classification of samples
- Accounts for sources of uncertainty that might be related to the shape, deformability, stability, or activity of objects in a liquid sample
- Does not require a microscope
- Compatible with on-chip sorting technologies



Serial cytometry involves making repeated measurements of single objects as they pass through multiple interrogation regions in a microfluidic channel. Integrated optical waveguides deliver and collect light from objects. Matching and analysis of signals from individual cells, for example, enable uncertainty estimates on the biomarker content of each cell, which enables better comparison and classification of cells and mixture of cells.

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NIST TECHNOLOGY PARTNERSHIPS OFFICE

NIST Technology Partnerships Office
National Institute of Standards and Technology
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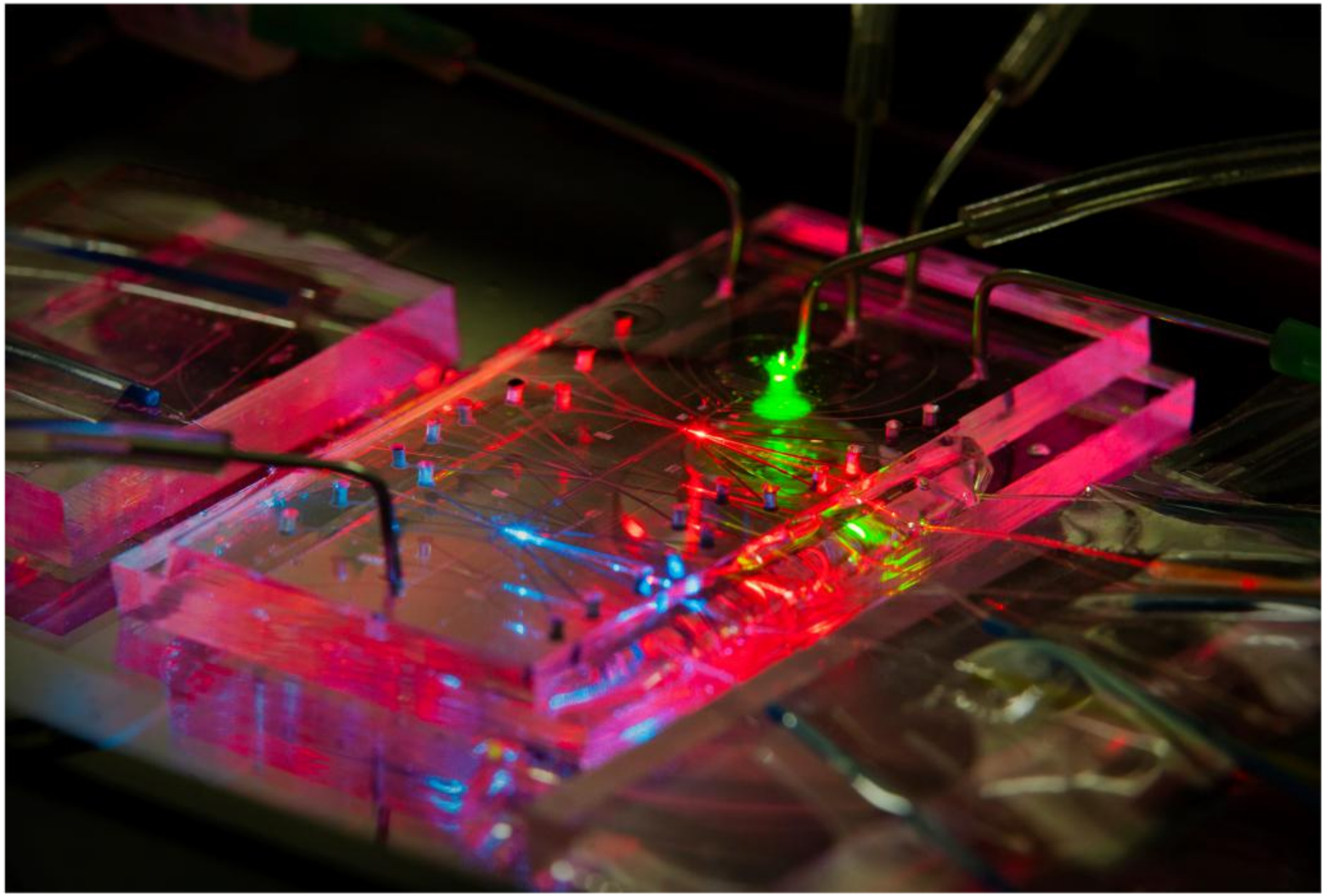
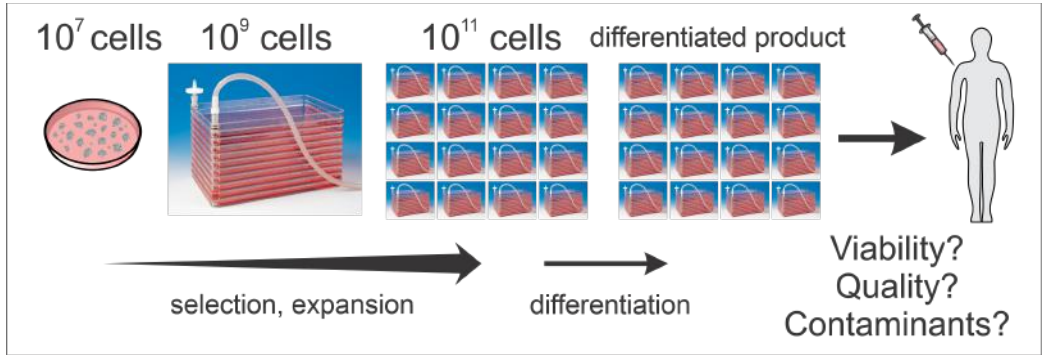
Serial Cytometry



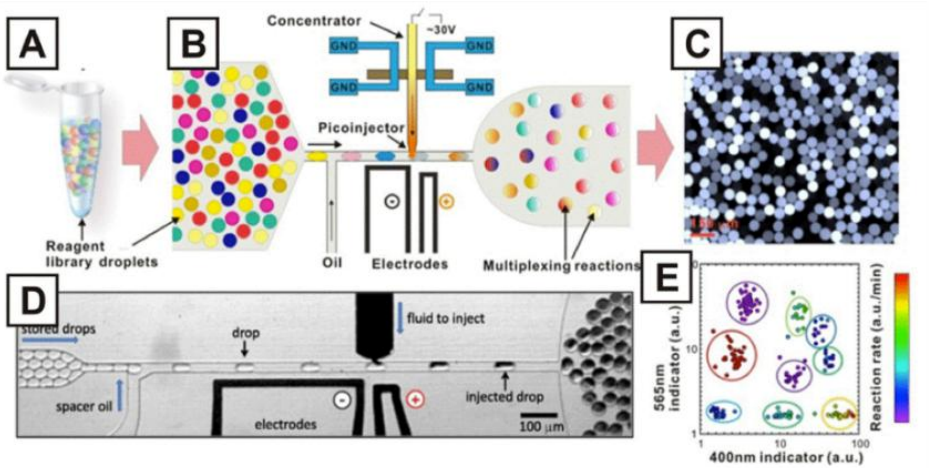
Challenges for High-Throughput Biometrology

Regenerative Medicine

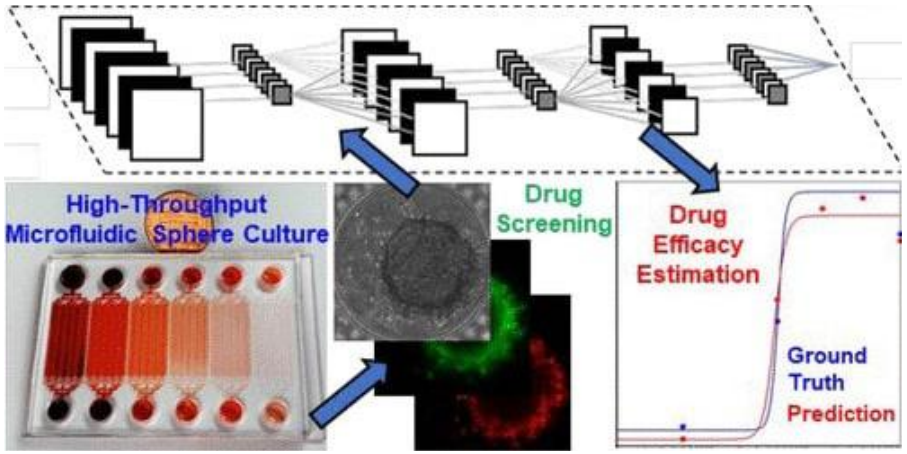


Cancer Screening

Drug Discovery



Drug Screening

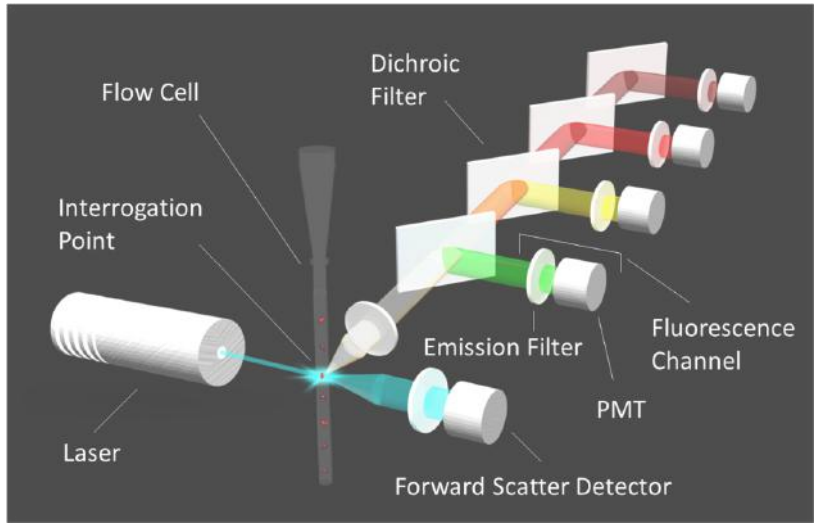


Yoon Lab, University of Michigan

Flow Cytometry Measurements

State-of-the-art

- **Measurement of cell characteristics, like size, and biomarker abundance, count and classification**
- **High throughput: 10,000 cells/s**
- **Used in cancer detection, drug development, biomanufacturing**
  - No robust theory of uncertainty, Not clear how to assess accuracy
  - Comparability is challenging
  - Classification is subjective
- **Limited ability to detect rare events (approx. 1 in 10,000)**



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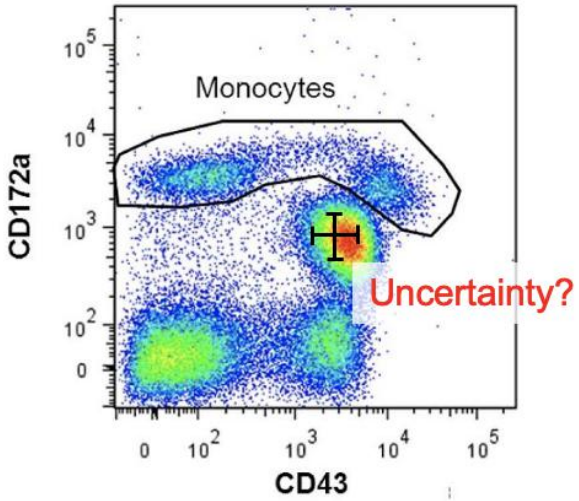
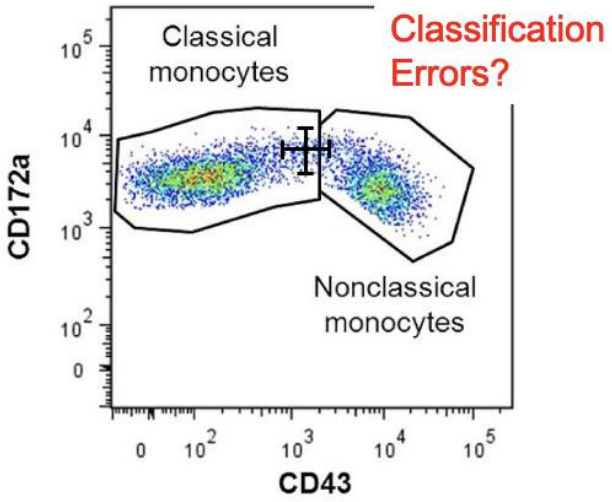
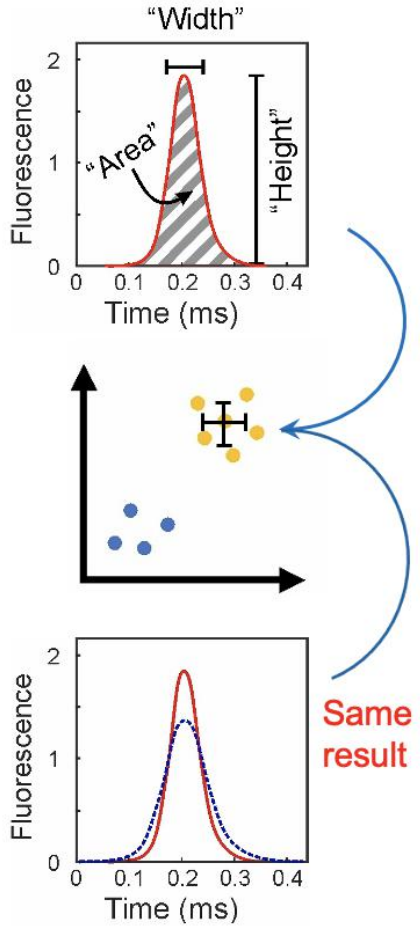
Why is Cytometry Hard?

Need a more robust strategy for uncertainty quantification

- **How can we compare one measurement to another?**
- **How do instrument control choices affect outcomes?**
  - flow rate & focusing, optics, amplifier gains
- **What do the measurements tell us about a population?**

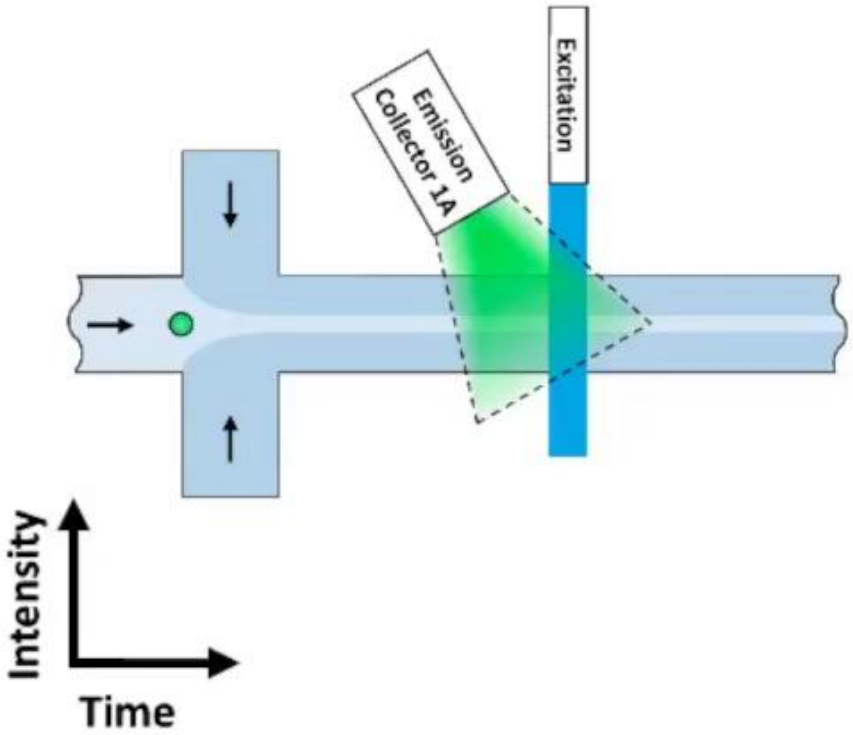




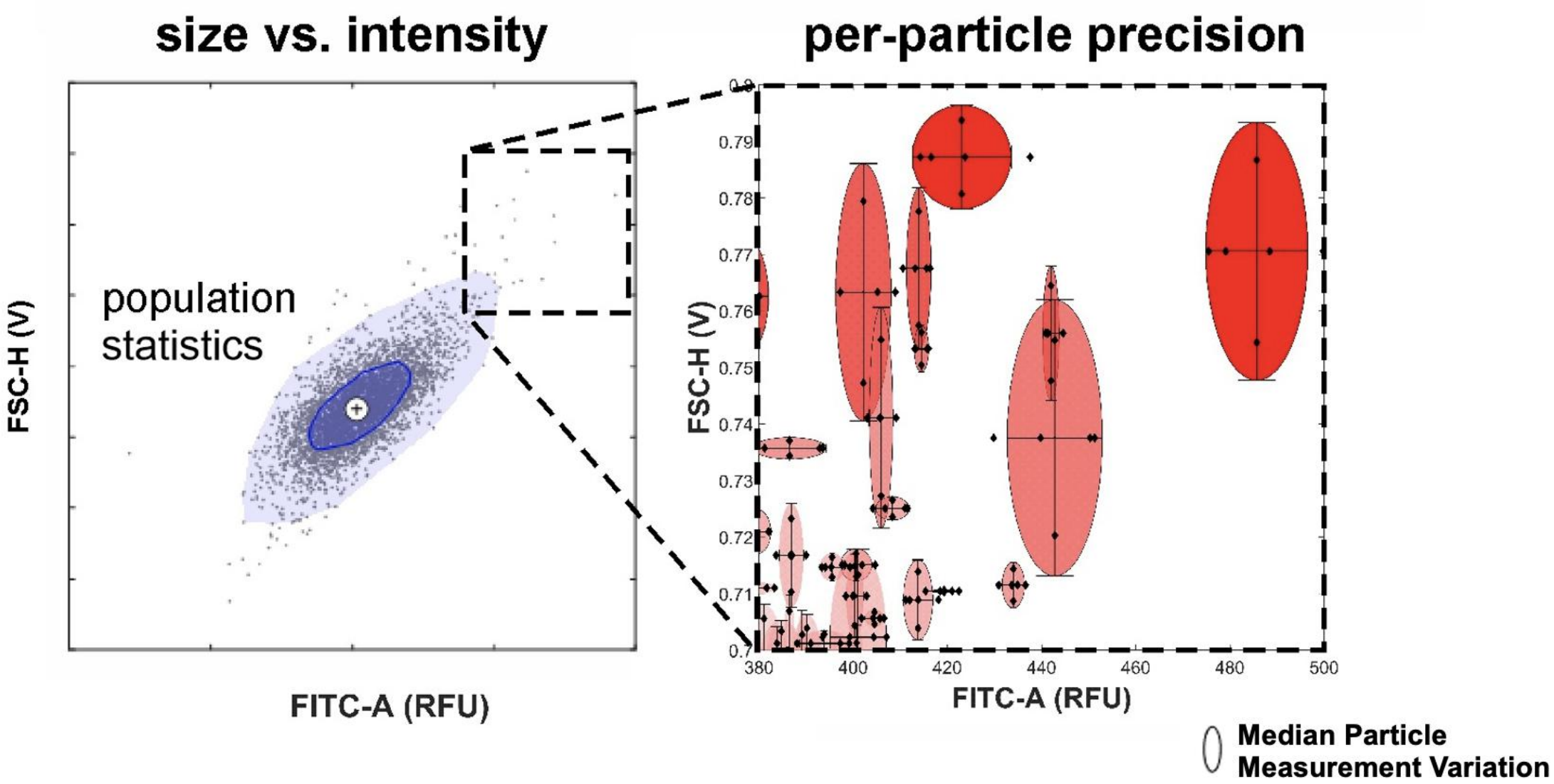


Serial Cytometry

Measurement Concept: Assessing Uncertainty through Repeated Measurements



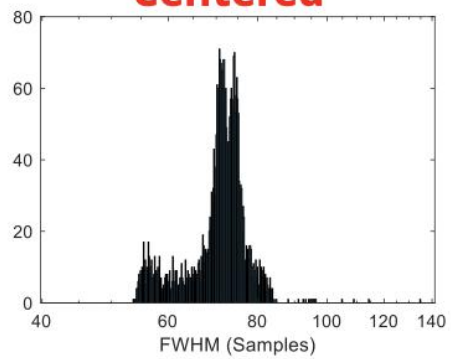
Per-particle Precision within a Population

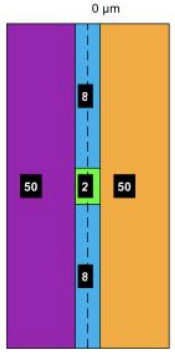


Real-time Assessment and Control of Data Quality

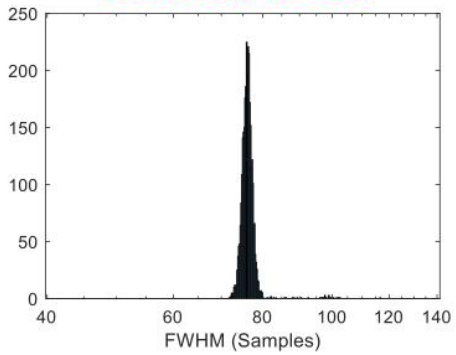
Stream Position

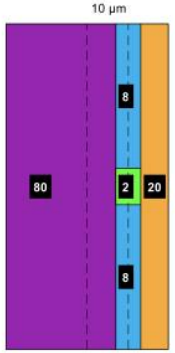
Centered





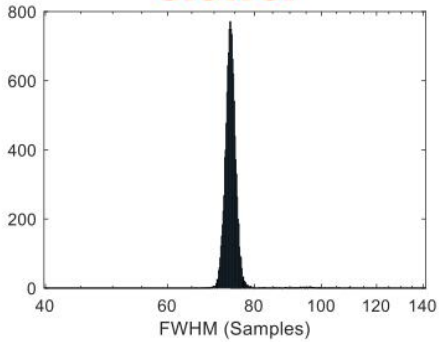
Inertial node

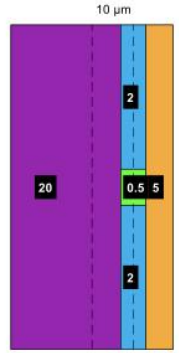




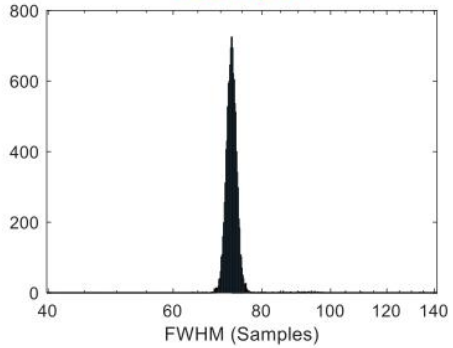
Velocity

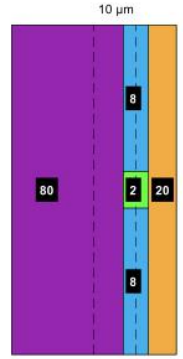
Slower



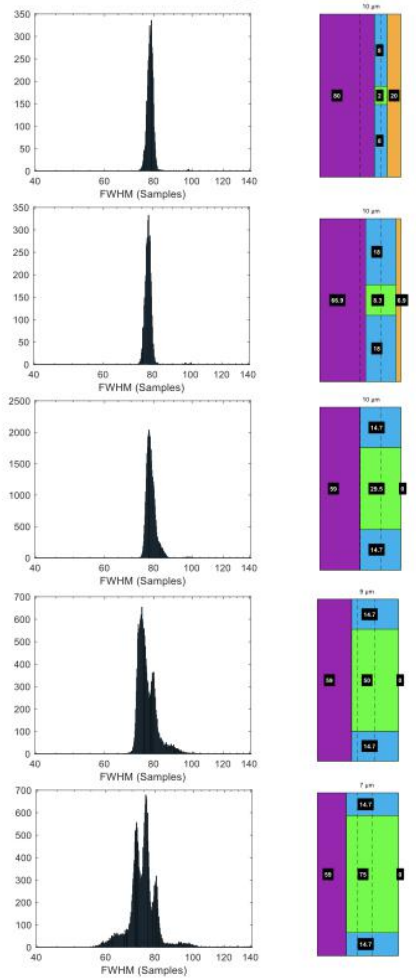


Faster





Focus Tightness



Serial Cytometry

Project Summary

- Serial Cytometry enables improved and new measurements
- Estimates of per-particle uncertainty experimentally and analytically, setting the stage for better classification
- Also enables innovation and optimization of system performance
- Signals analysis to study deformability,discriminate doublets
- Working on metrics to improve detection and classification (rare event detection, other specs)
  - <100 MESF Limit of Detection
  - <1% relative uncertainty
  - 1 in 10,000 tracking error
  - 500 events per second