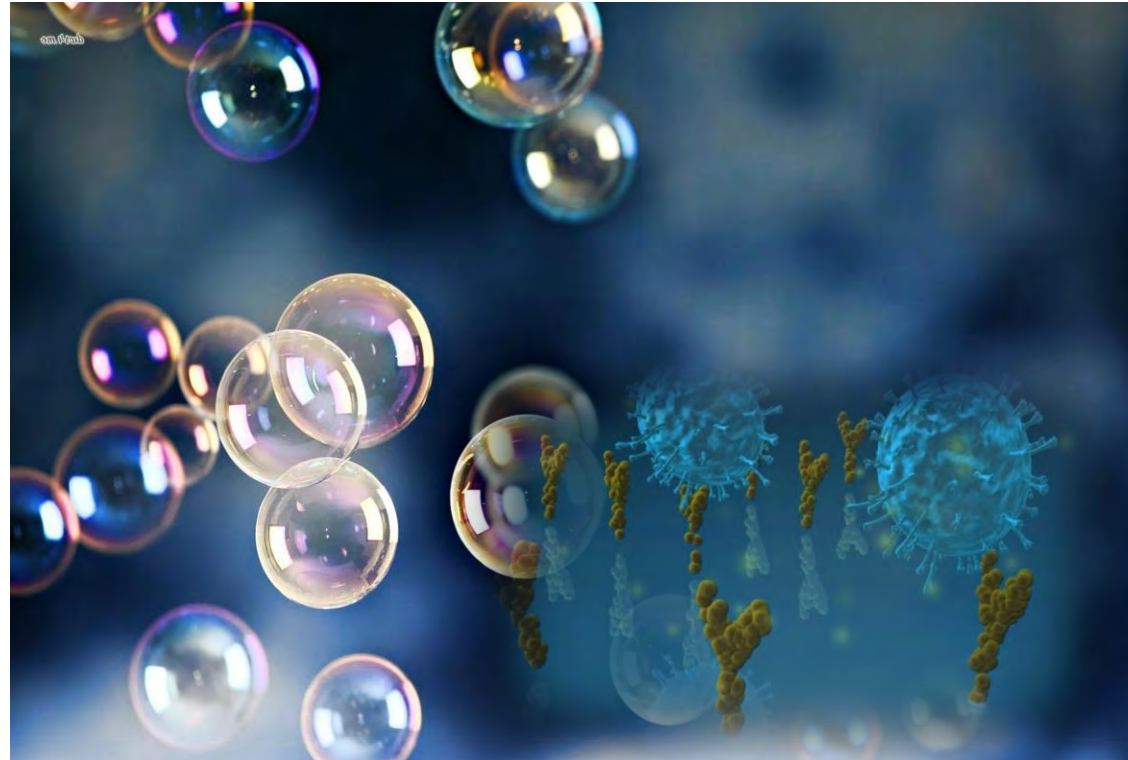


Enhanced Detection and Visualization of Exosomes with Interferometric Reflectance Imaging

M. Selim Ünlü

Electrical Engineering,
Physics,
Biomedical Engineering
Graduate Medical Sciences

- Detection vs. visualization/characterization
- Interferometric Reflectance **Imaging** Sensor
- Biological Nanoparticle Detection and Sizing
- In-liquid detection
- Pupil function engineering
- Resolution improvement by oblique illumination and reconstruction
- Towards 100nm in label-free visible light microscopy



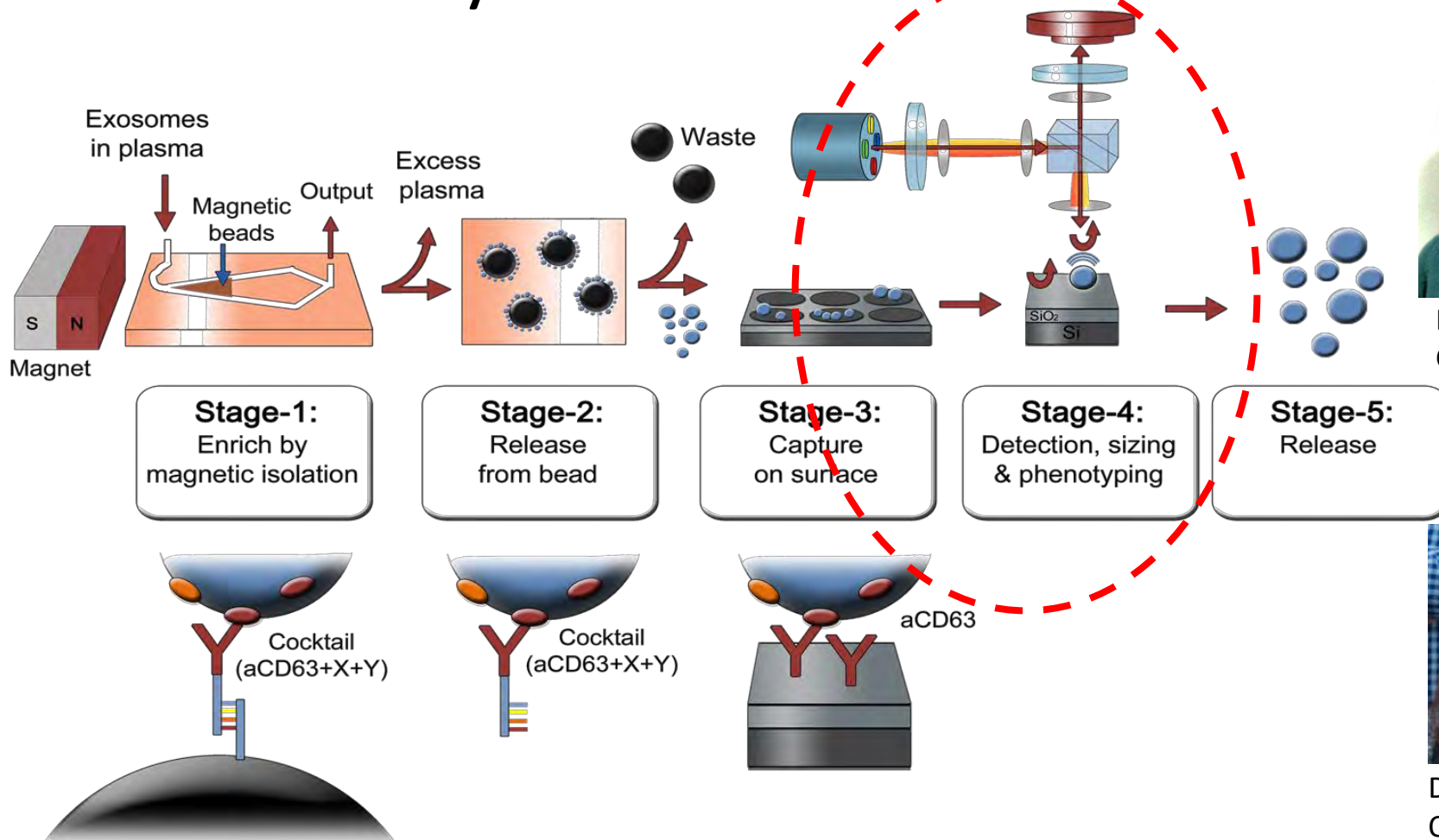
Integrated nanoparticle isolation and detection system for complete on-chip analysis of exosomes



Dr. Marcella Chiari



Dr. Ayca Yalcin Ozkumur



Interferometric Reflectance Imaging Sensor (IRIS)

- a versatile multiplexed platform

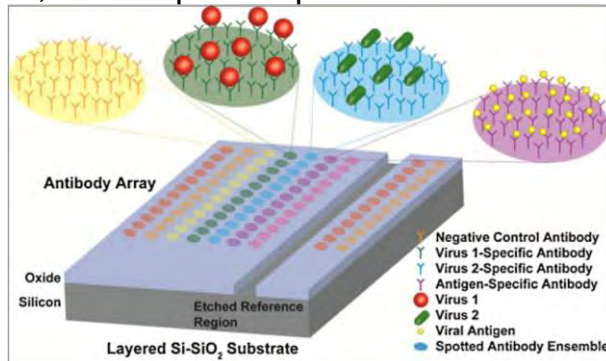
soap film



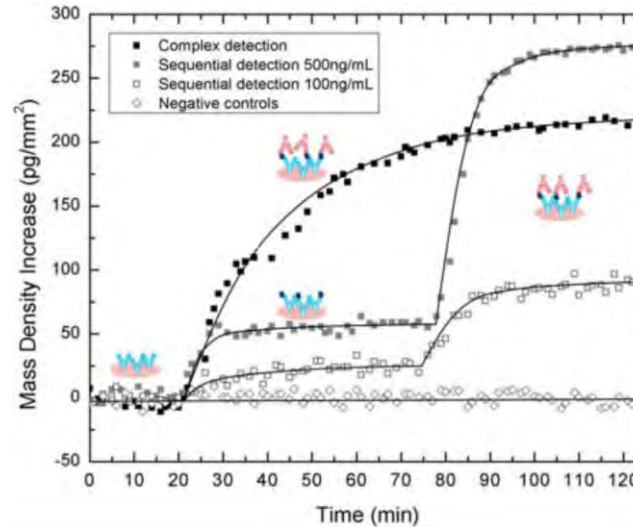
Oxide coated Si



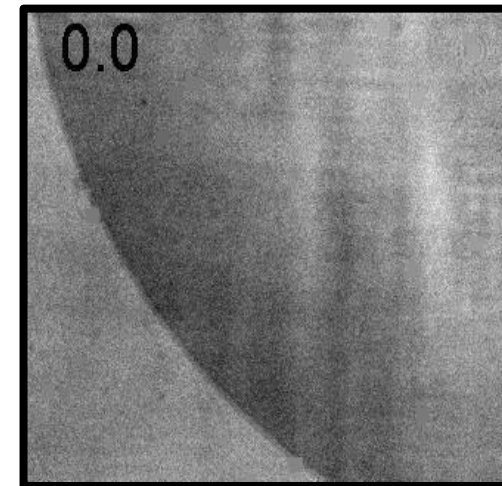
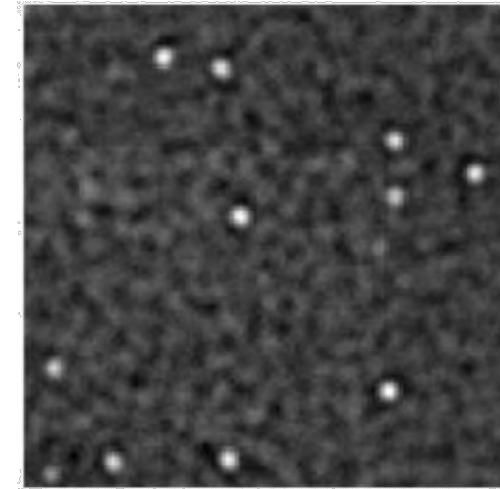
Protein microarray chips with 100s to 1,000s of probe spots



Kinetic Measurements
Molecular Binding

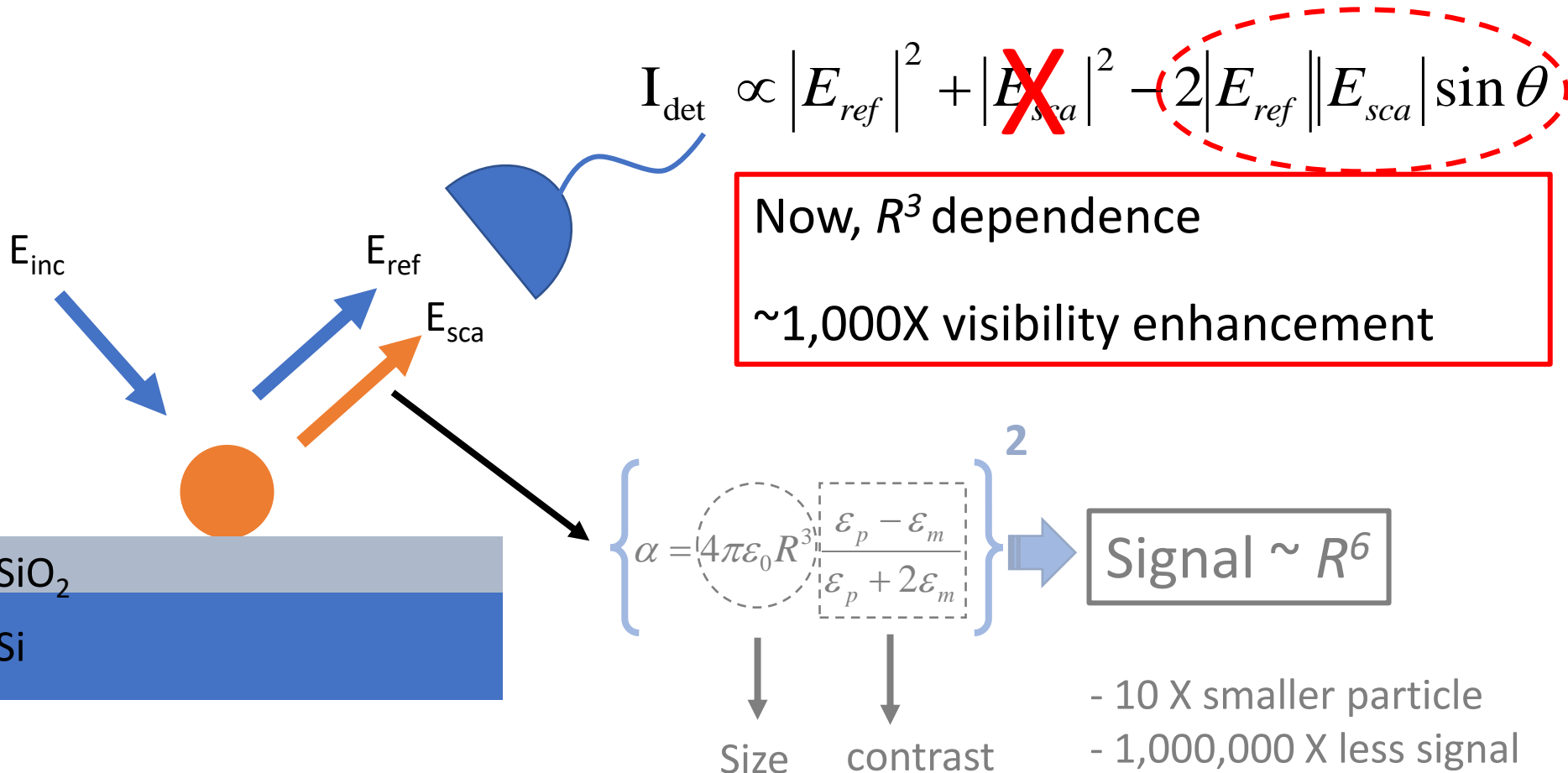


Single virus/exosome
Detection/visualization



Nanoparticle Detection and Sizing

Why difficult and how we make it easy



Single Exosome Detection



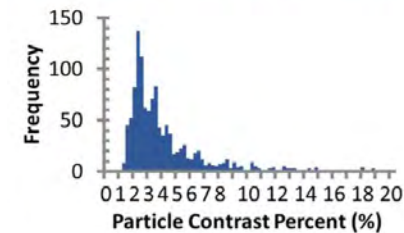
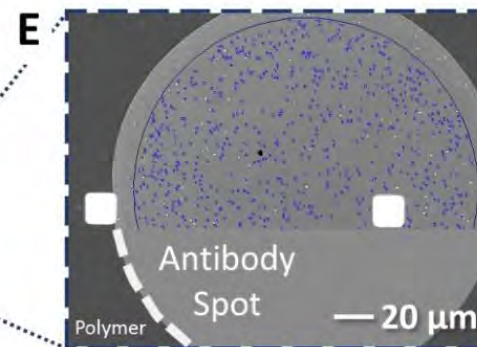
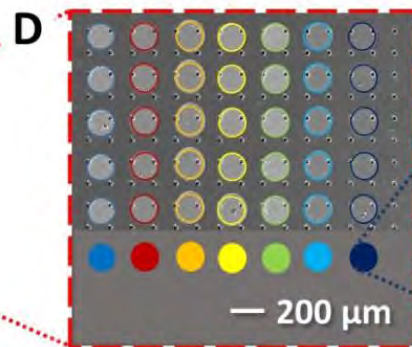
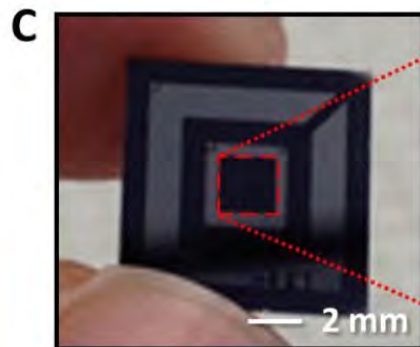
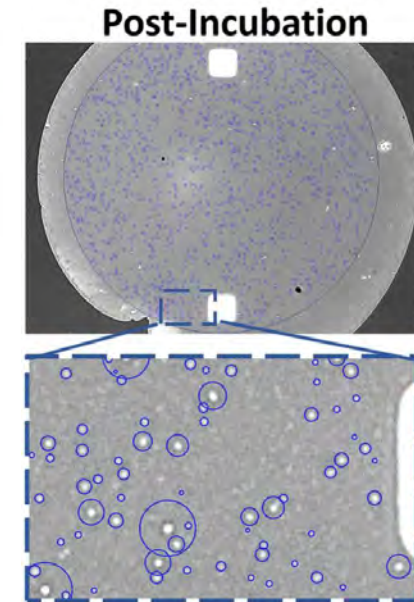
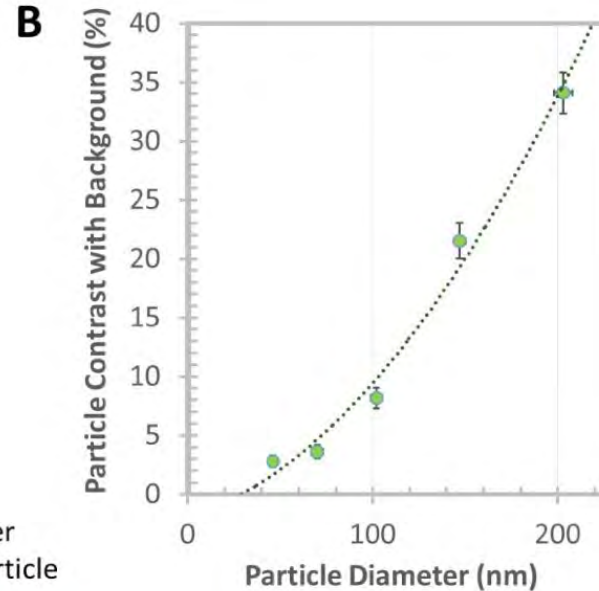
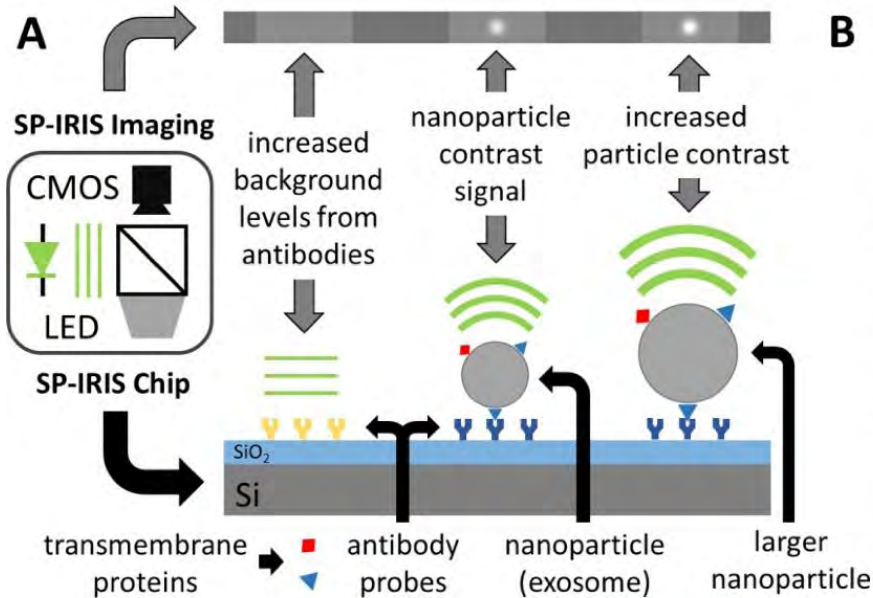
Daaboul '13

OPEN

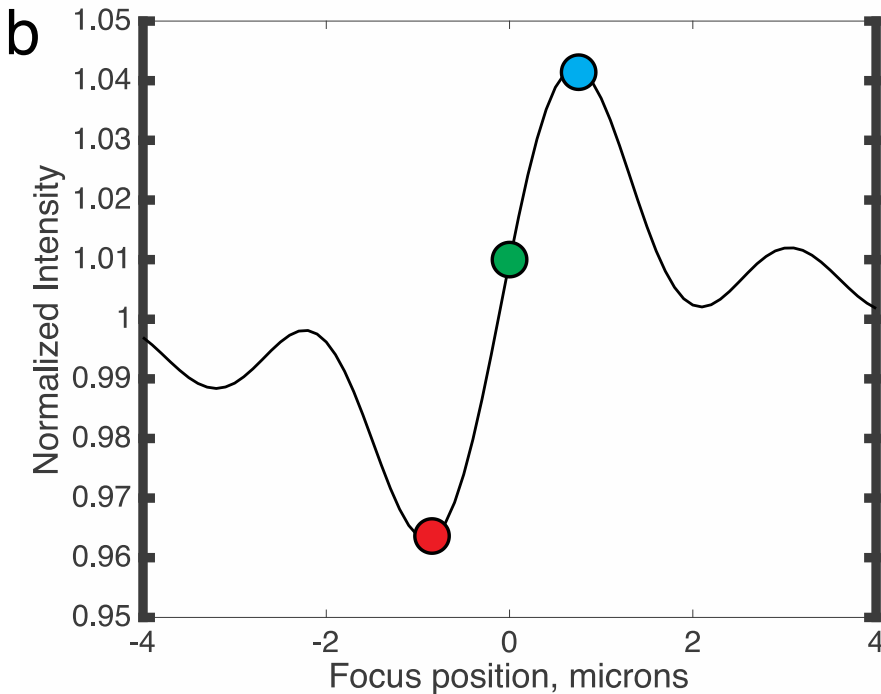
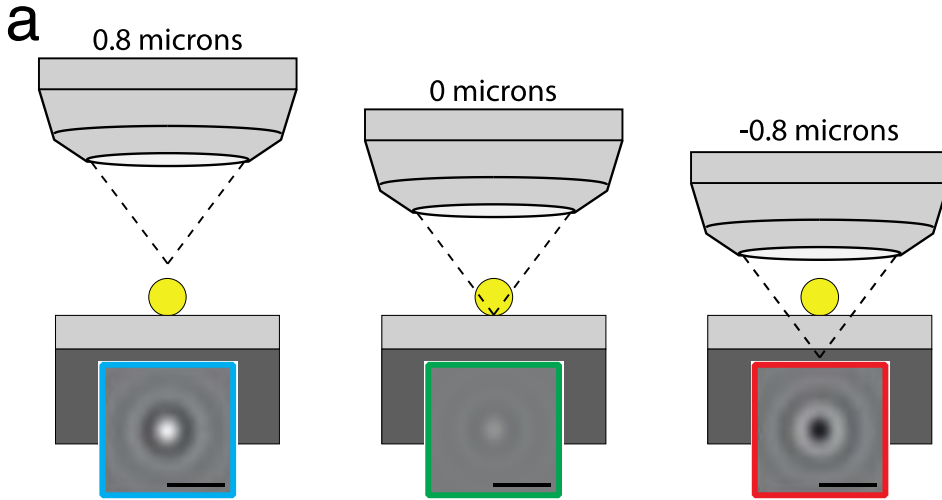
Digital Detection of Exosomes by Interferometric Imaging

George G. Daaboul^{1,*}, Paola Gagni^{2,*}, Luisa Benussi³, Paolo Bettotti⁴, Miriam Ciani³, Marina Cretich², David S. Freedman¹, Roberta Ghidoni³, Ayca Yalcin Ozkumur⁵, Chiara Poggio⁴, Davide Prosperi⁶, Benedetta Santini⁶, M. Selim Ünlü⁷ & Marcella Chiari²

Received: 20 June 2016



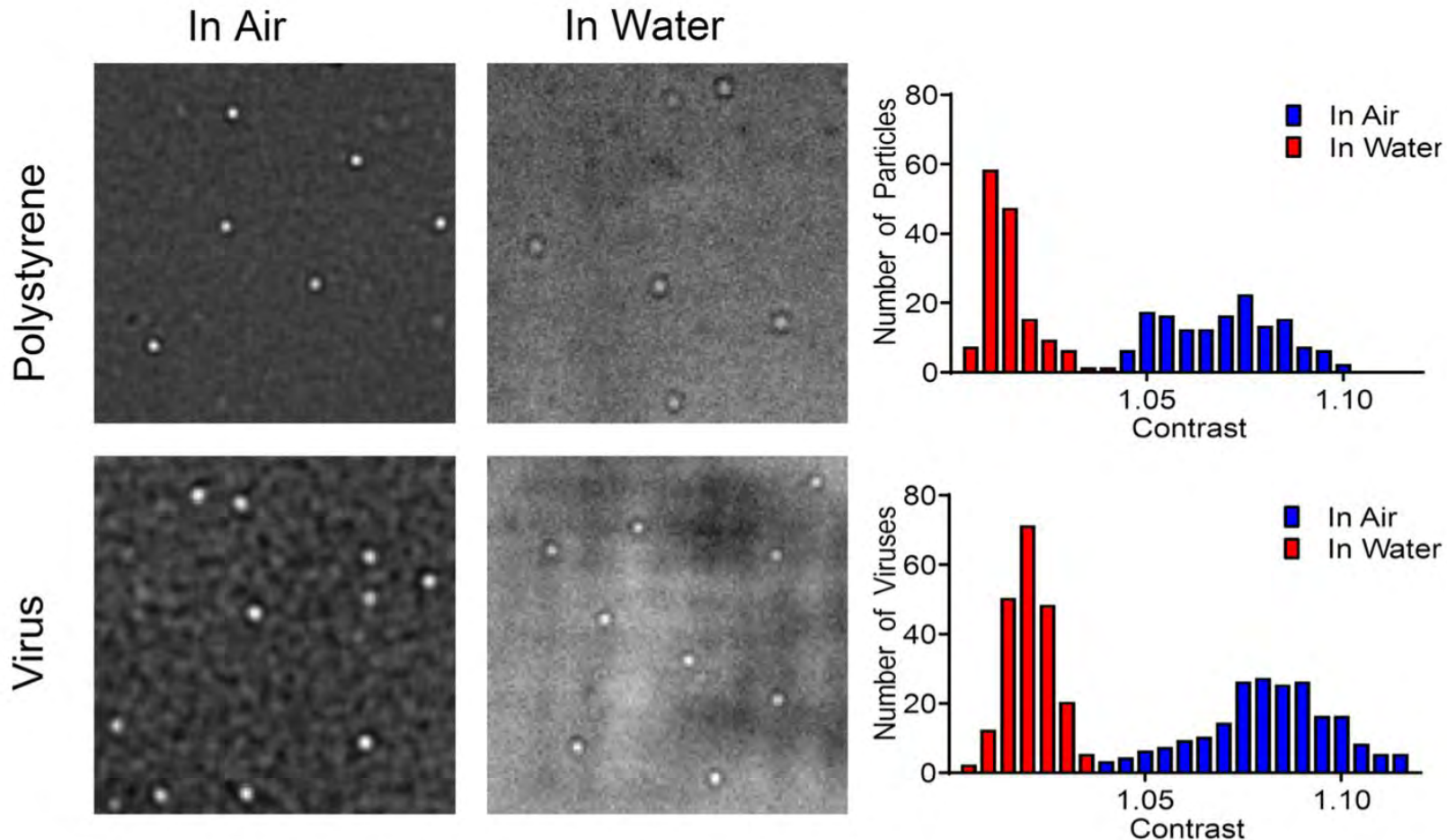
Accurate Sizing – defocus profile



$$I_{\text{det}} \propto |E_{\text{ref}}|^2 + |E_{\text{sca}}|^2 - 2|E_{\text{ref}}||E_{\text{sca}}|\sin \theta$$

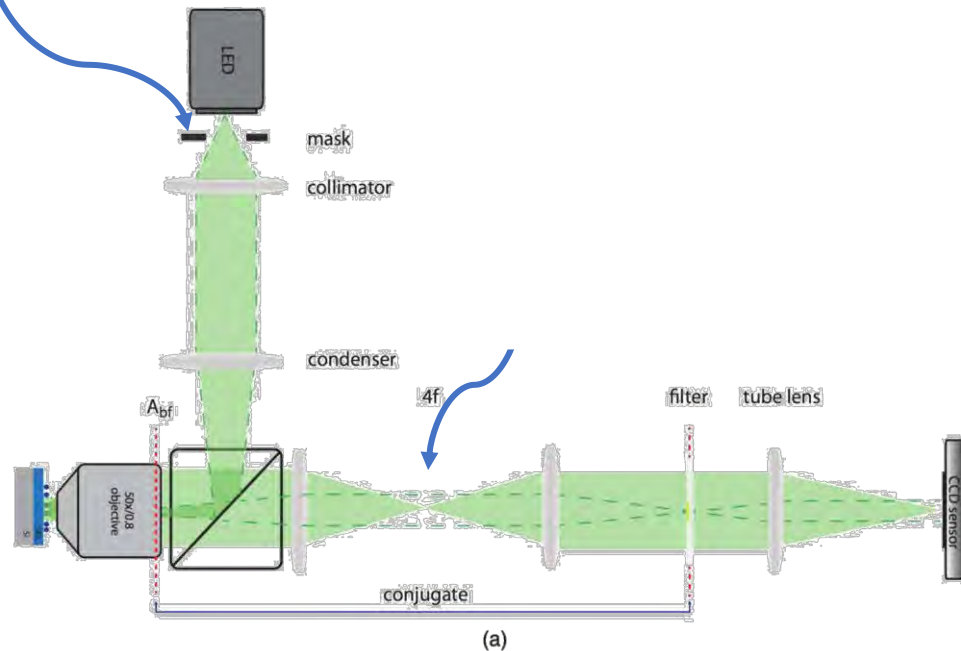
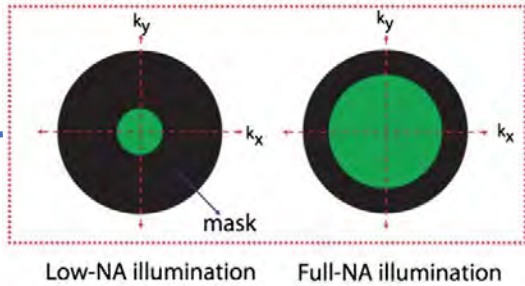
Changing the focus position changes the path length to the detector differently for reference reflection and scattered light

In-liquid detection offers a more versatile assay, but challenges exist

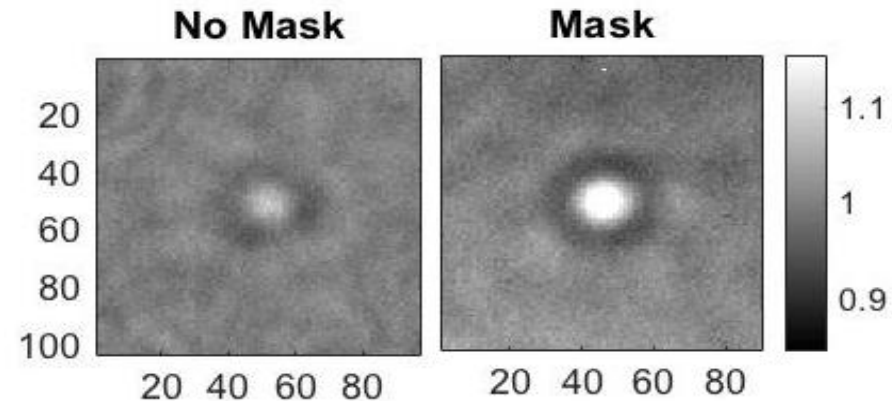
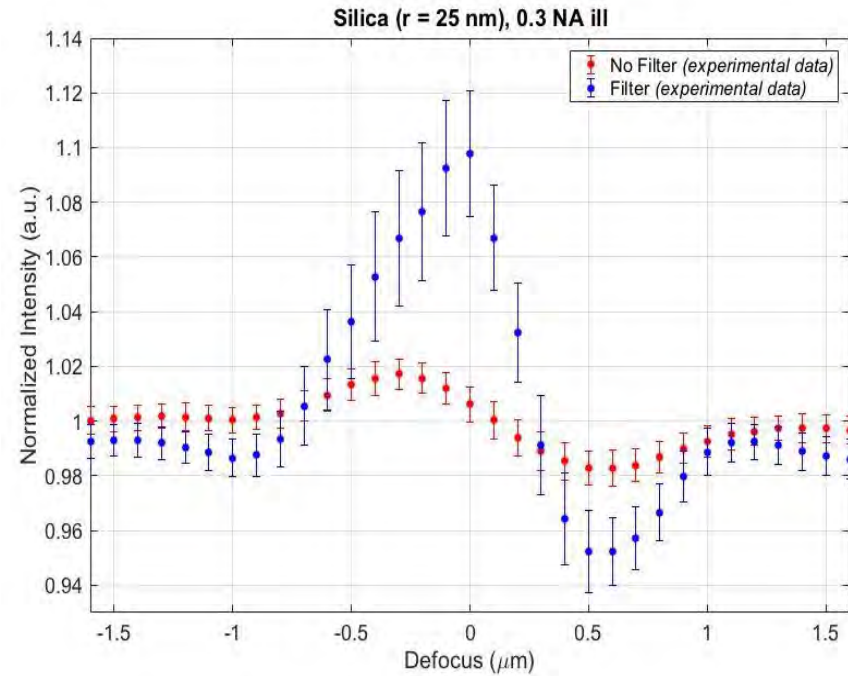


Pupil function engineering for enhanced nanoparticle visibility in wide-field interferometric microscopy

Objective back focal plane aperture

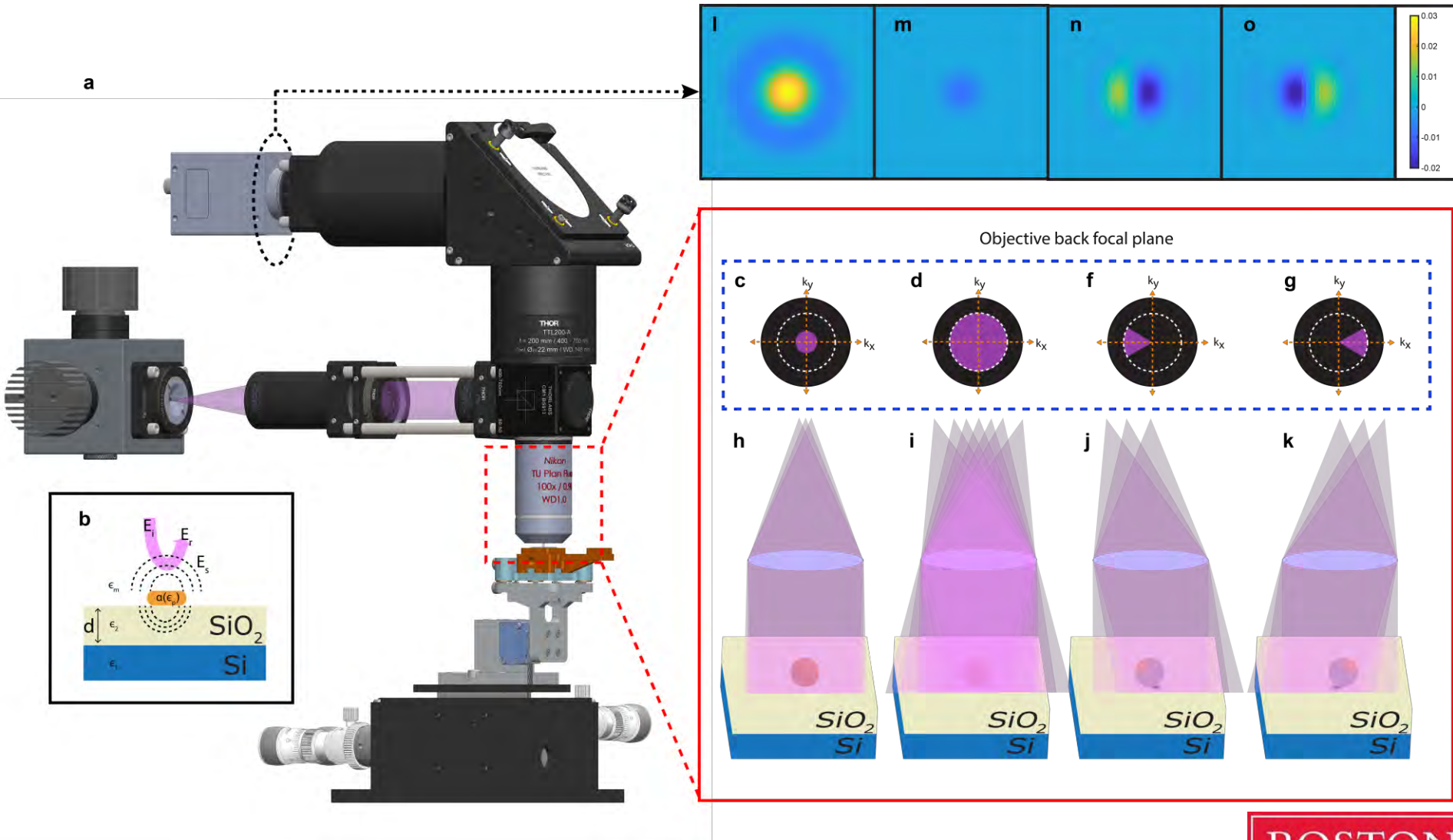


(a) Collection Path – Apodization and Reference Attenuation

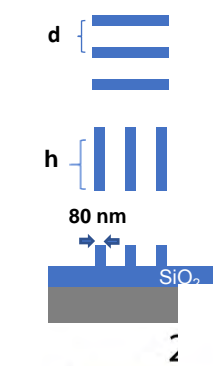


Contrast enhancement of Silica particles with $r=25 \text{ nm}$ using pupil function engineering.

Super-resolution in wide-field interferometric microscopy



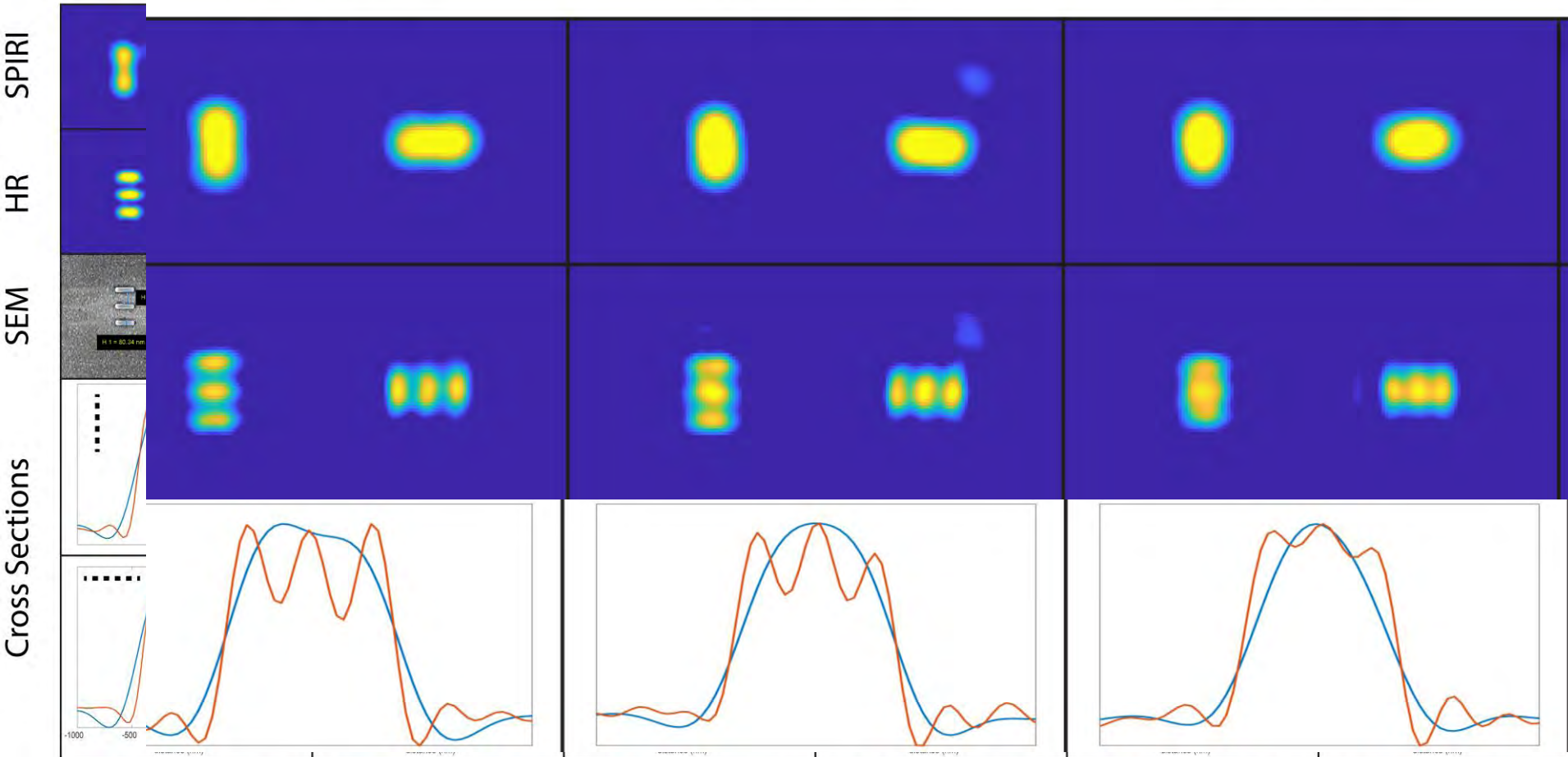
Reconstructed resolution targets



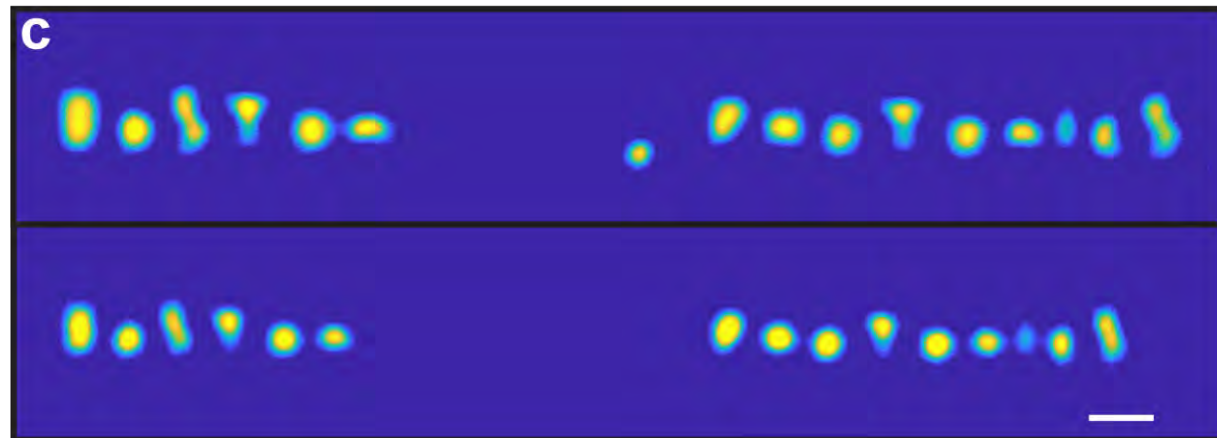
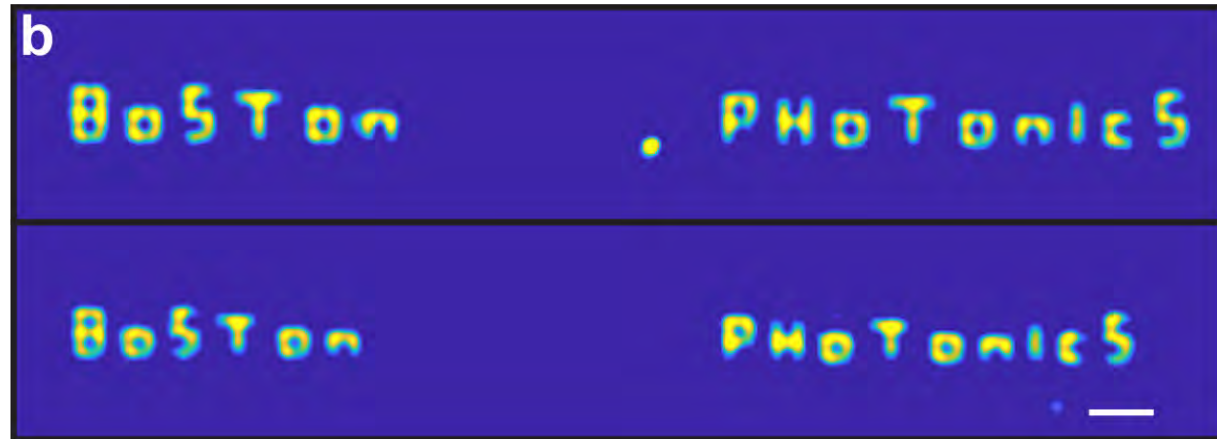
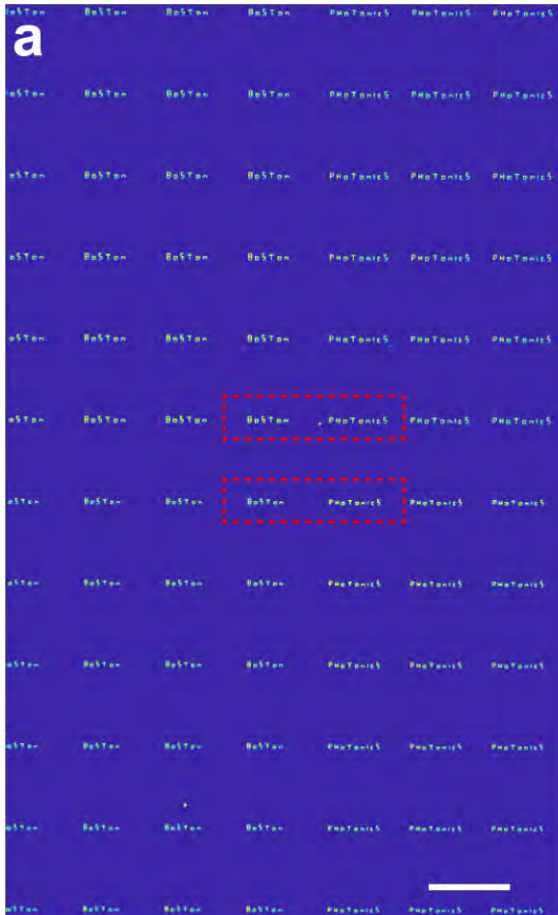
175 nm

150 nm

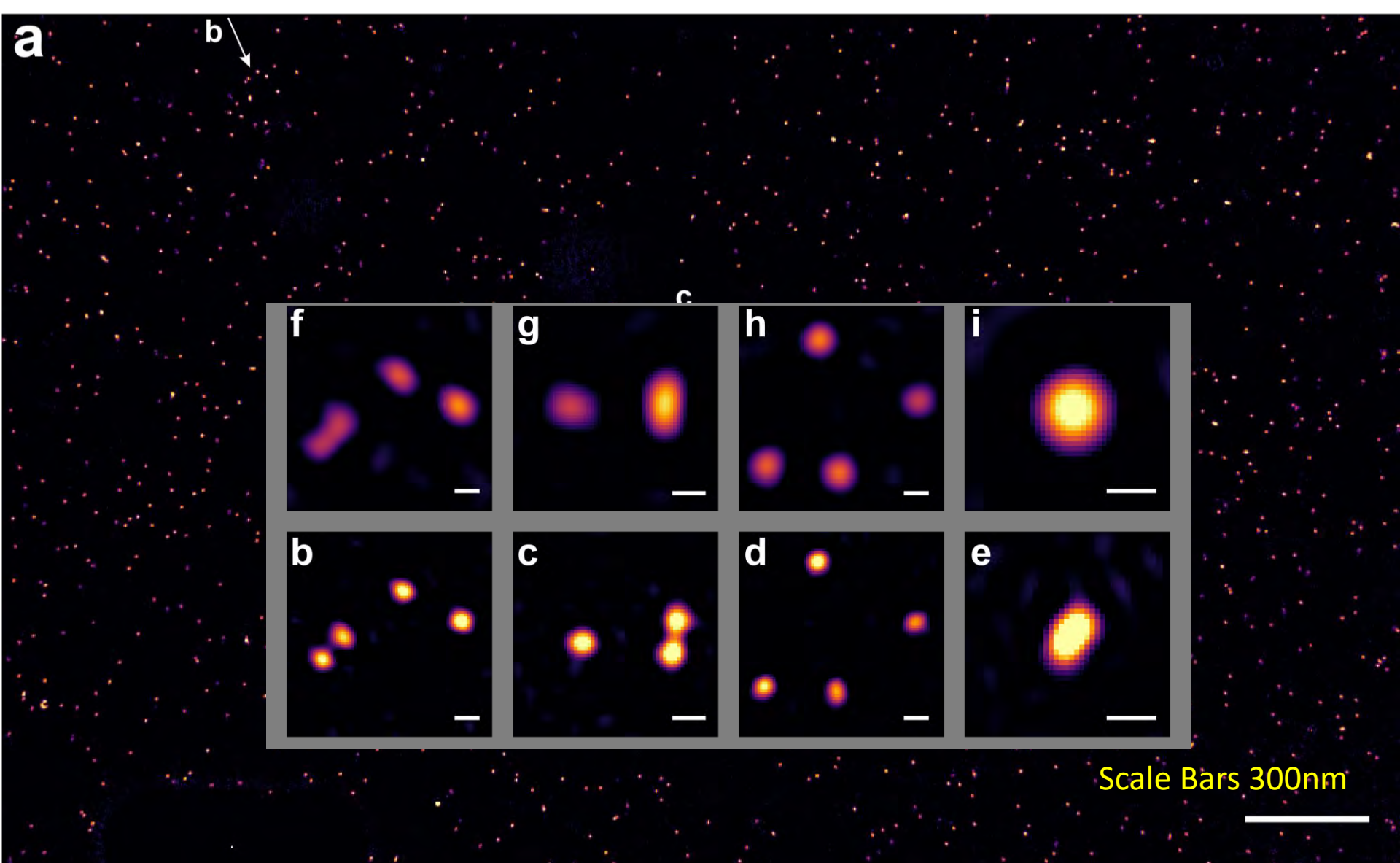
125 nm



Wide-field Imaging/Reconstruction

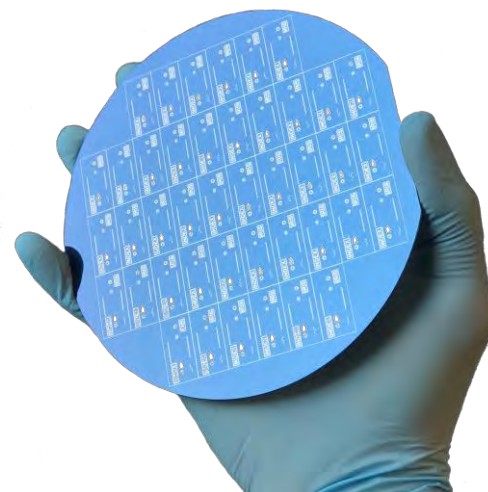
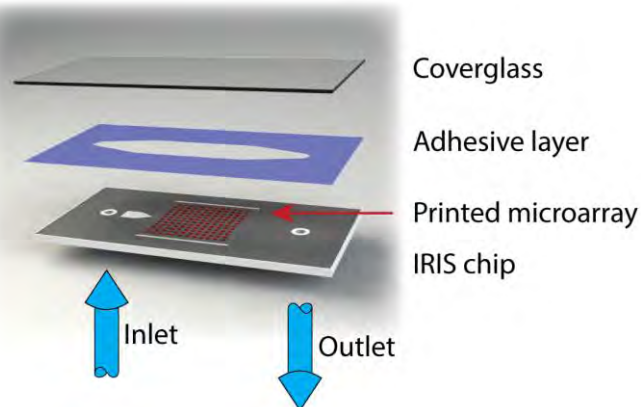
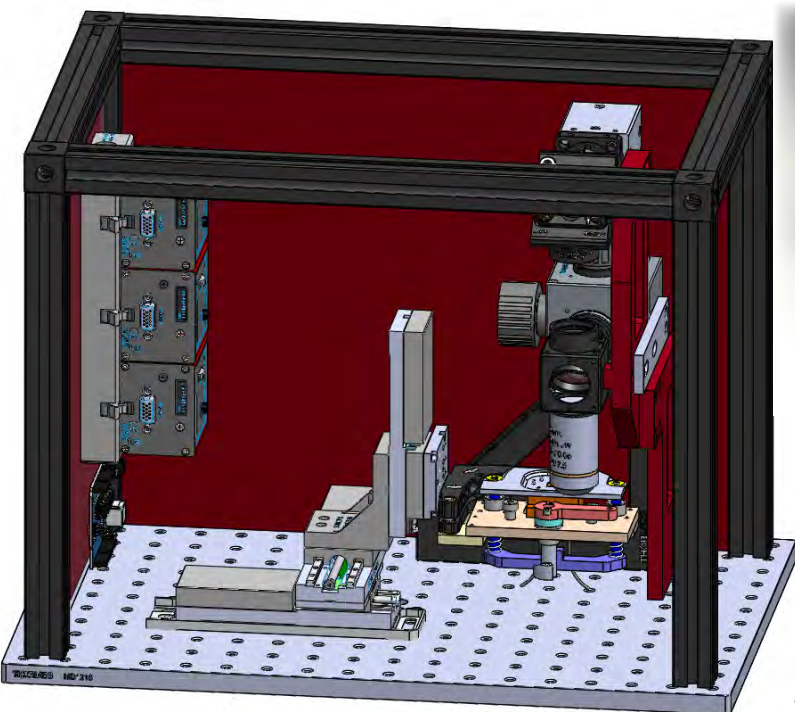


Scale Bars are 10 micron and 1 micron



< 150 nm lateral resolution with > 120 micron Filed-of-view

Chips, Si-based Microfluidics, Prototype Instrument



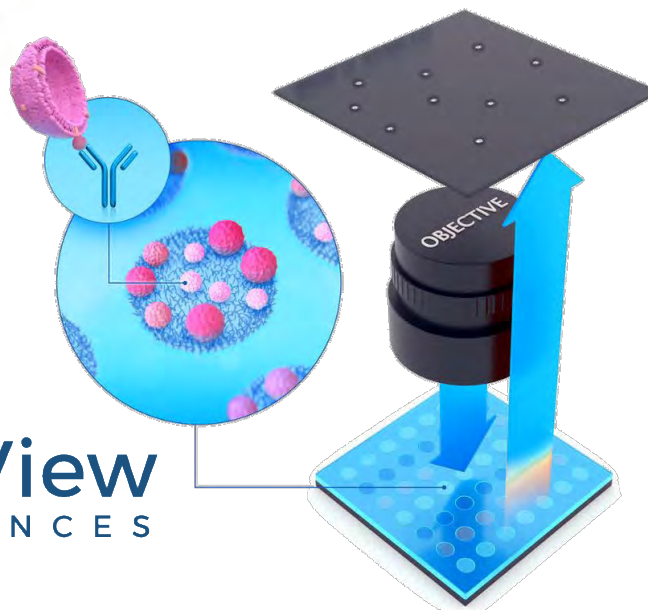
Interferometric Detection and Enumeration of Viral Particles using Si-based Microfluidics

Ayca Yalcin Ozkumur, Fulva Ekiz Kanik, Jacob Trueb, Celalettin Yurdakul, and M. Selim Ünlü,

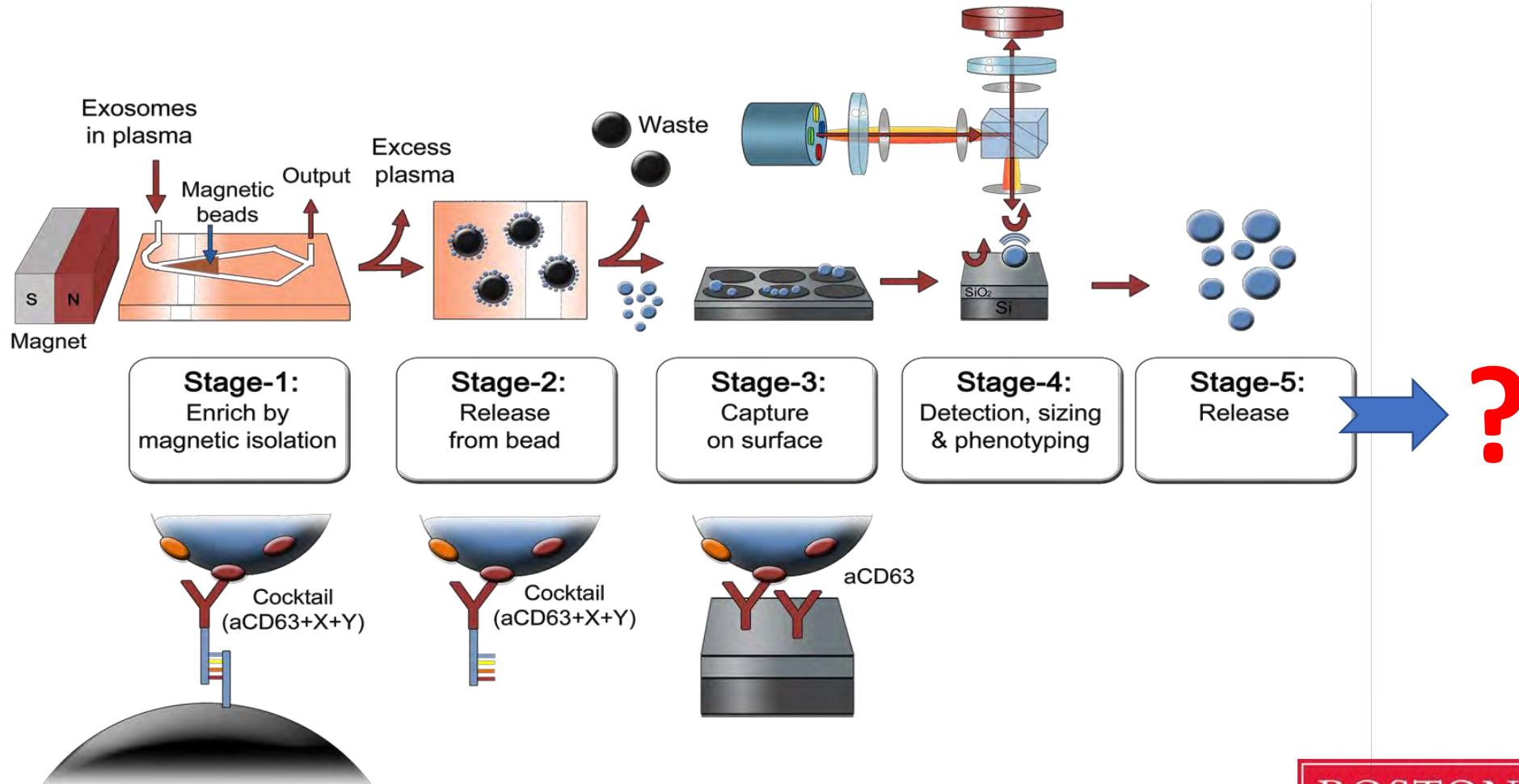
IEEE JSTQE 2019



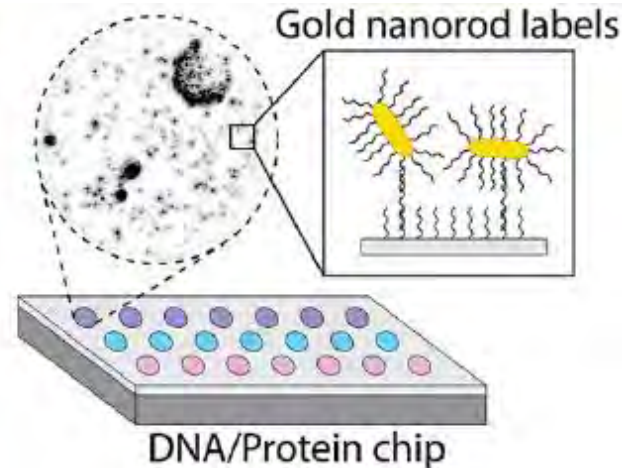
NanoView
BIOSCIENCES



Integrated nanoparticle isolation and detection system for complete on-chip analysis of exosomes



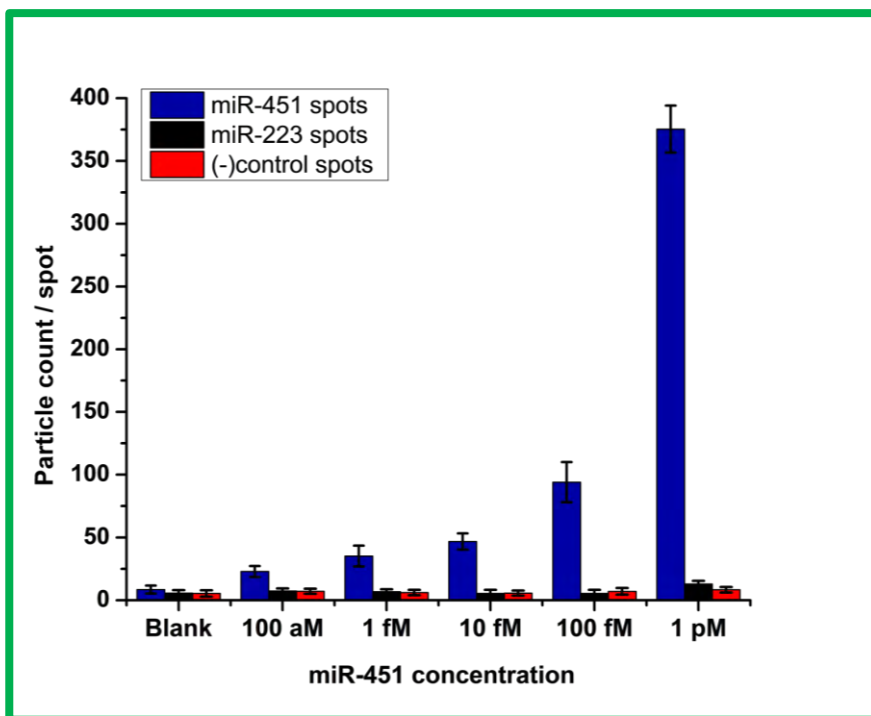
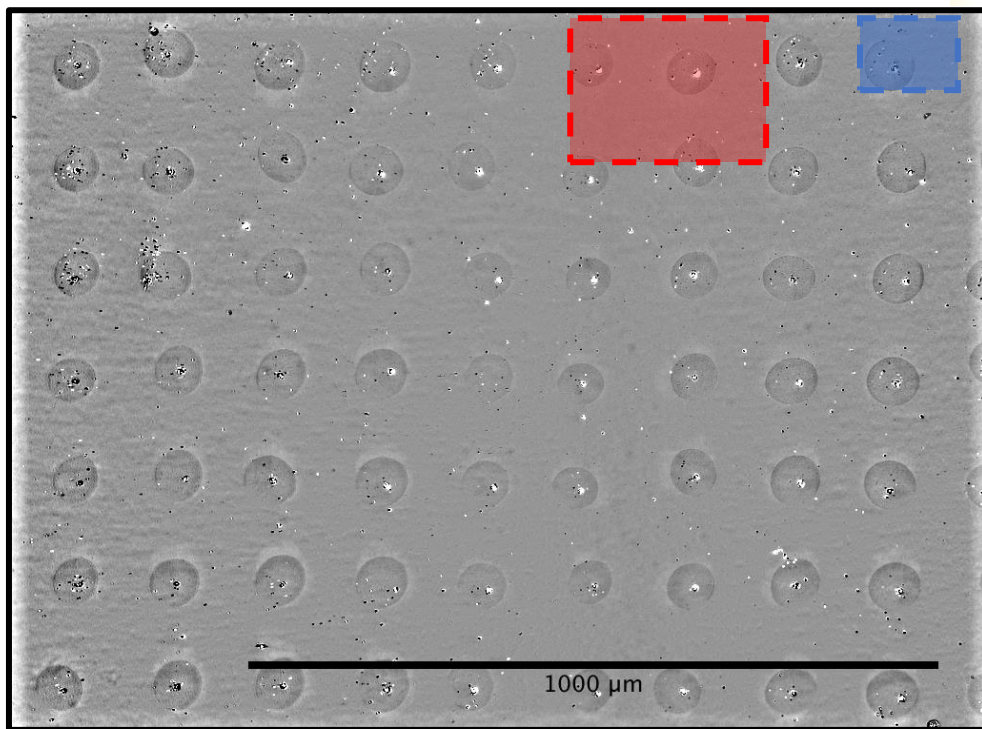
Digital Microarrays: Single-Molecule Readout with Interferometric Detection of Plasmonic Nanorod Labels



10x Objective

... 50x

... 100x



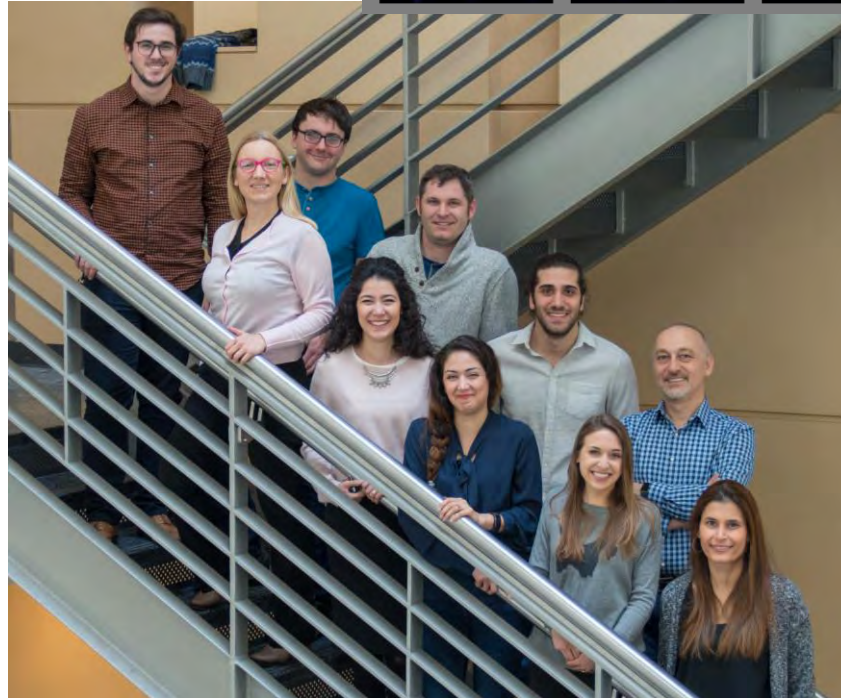
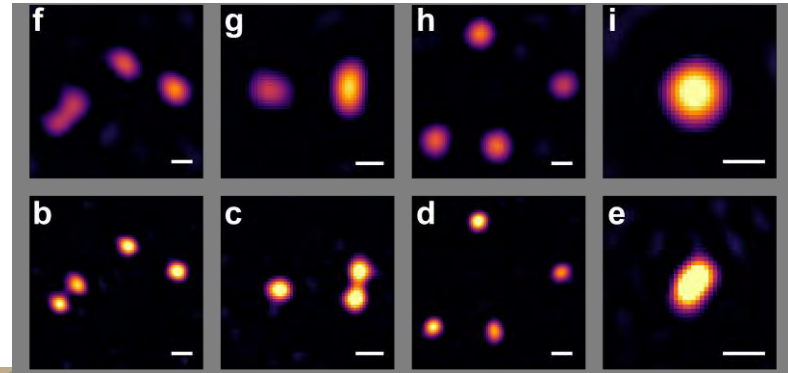
Detecting minute changes in cardiac biomarkers – at-risk patients identified earlier in their disease progression to guide more personalized care. miR-451 is a cardiac biomarker. Work in collaboration with Umass Medical.

CONCLUSIONS & FUTURE

Boston

PHOTONICS

- Optical interference is a very powerful measurement technique.
- Single biological nanoparticle detection / counting / size and shape discrimination / visualization
- **Goals:** Down to $r=20\text{nm}$
Biological nanoparticle detection in liquid
- Lateral resolution of $\sim 100\text{nm}$ without labeling



indEx

NanoView
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