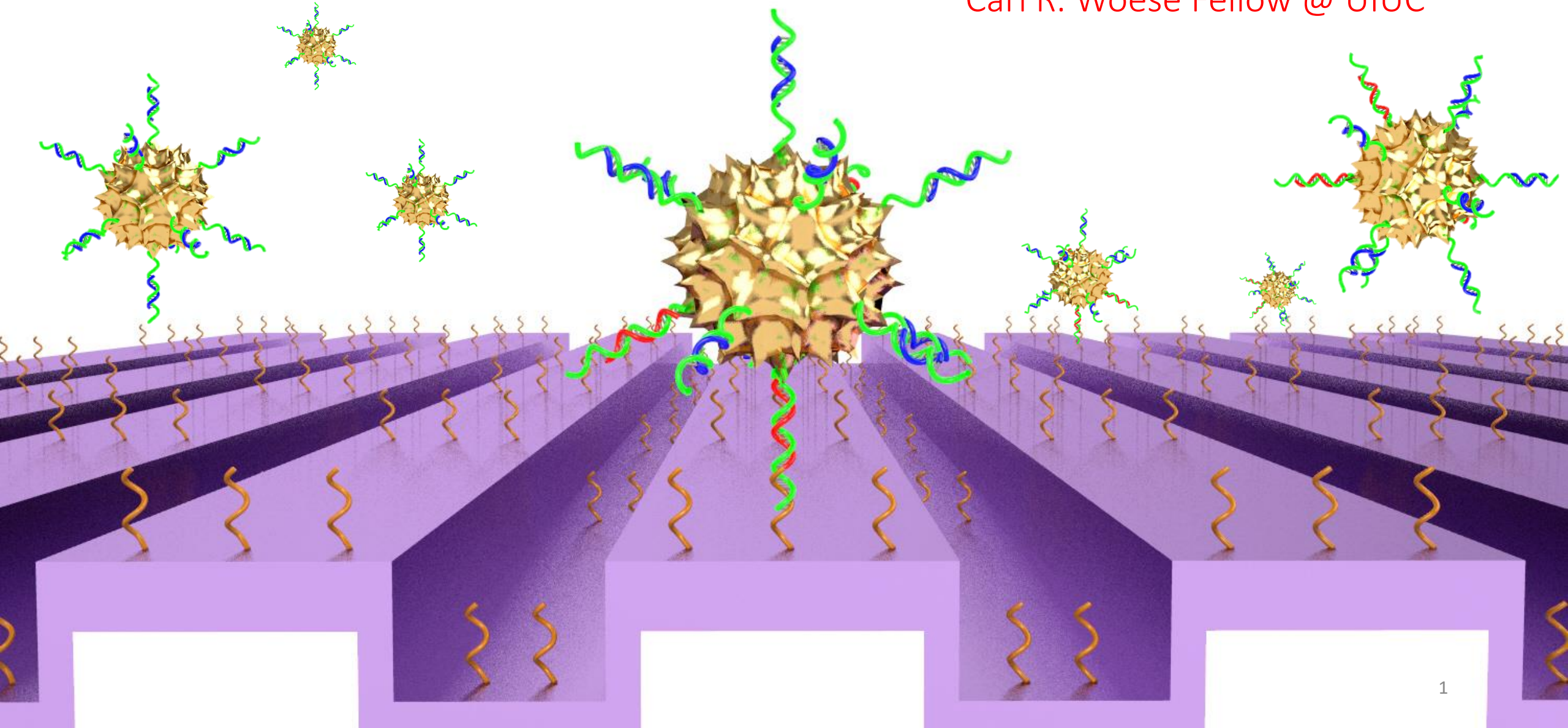


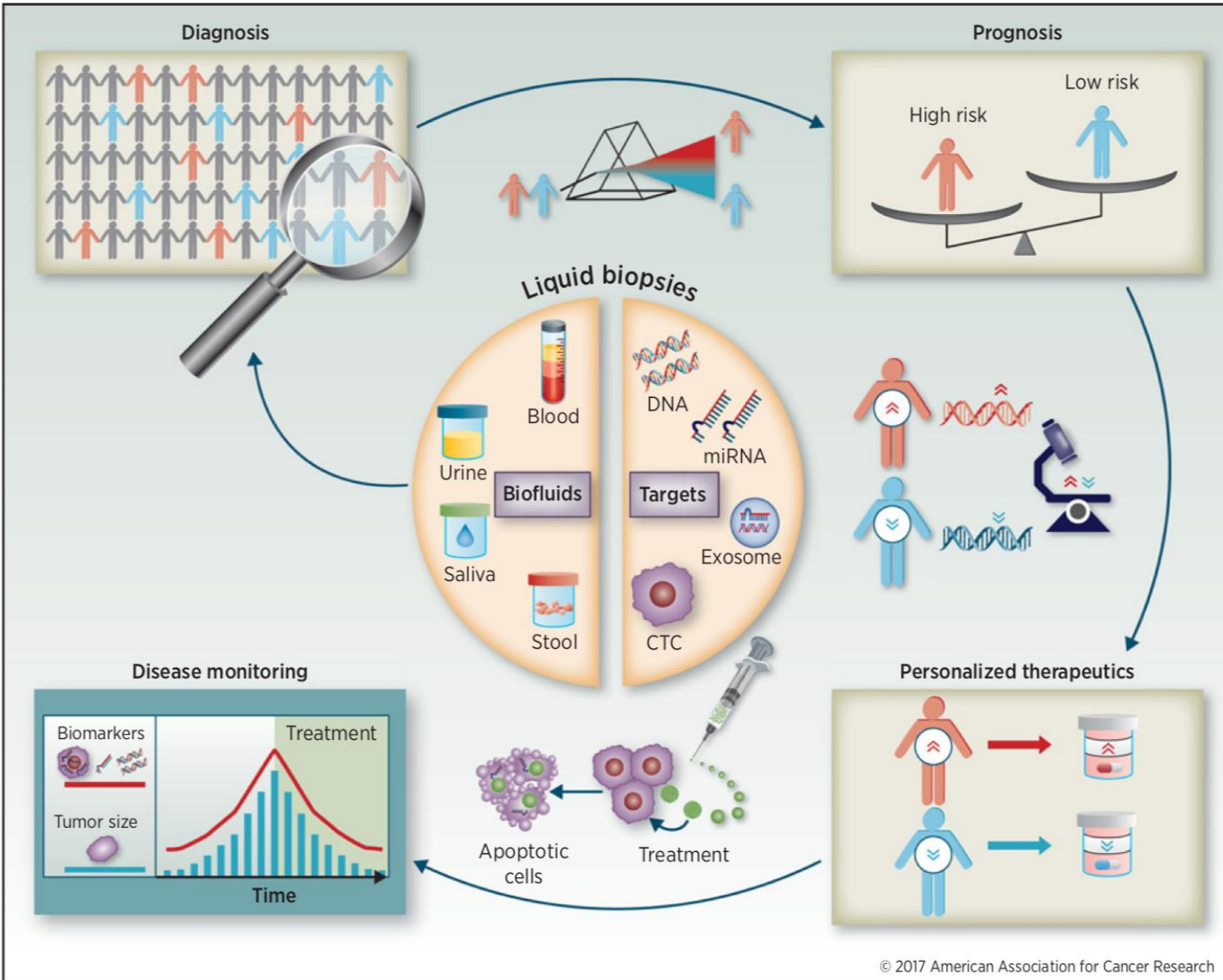
Detection of miRNA by Active Capture + Digital Counting (AC+DC) Microscopy

Taylor Canady

Carl R. Woese Fellow @ UIUC



Liquid Biopsy: Biofluid Biomarker Detection



Opportunity of Liquid Biopsy

- Non-invasive
- Early detection & quantification
- Sort mutation types
- Fast monitor and improve treatment

Challenges of Liquid Biopsy

- Targets \leftrightarrow Disease \leftrightarrow Patient Diversity
- Sequence similarity (SNPs)
- Concentration & matrix
- Build POC assay compatibility (time, cost, ...)

Design Constraints

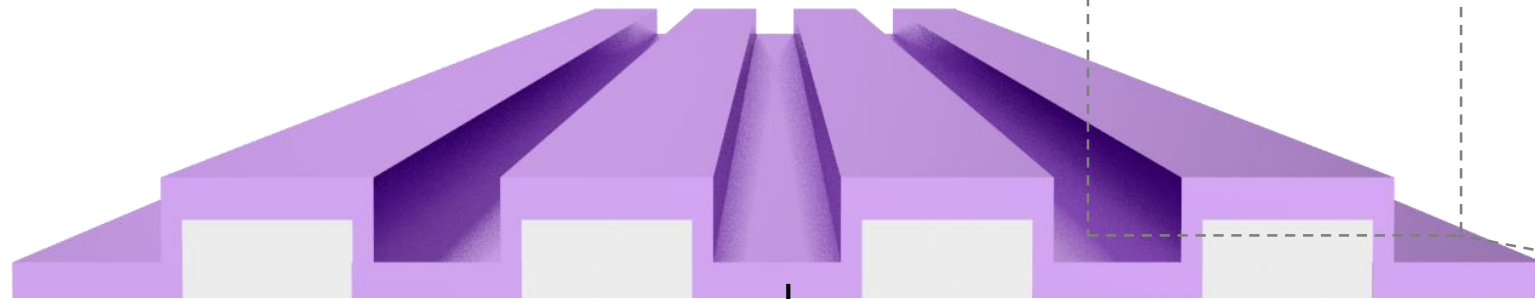
- Broad single base selectivity (DNA Nano)
- Extreme sensitivity (PC Biosensors)
- Wide dynamic range
- No amp, no wash
- Assay time: minutes to few hours

Engineering Tools for liquid Biopsy of miRNA Biomarkers

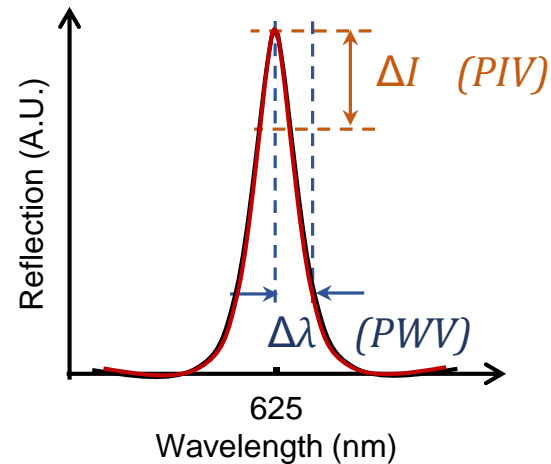
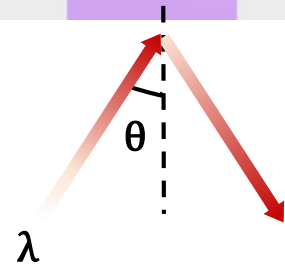
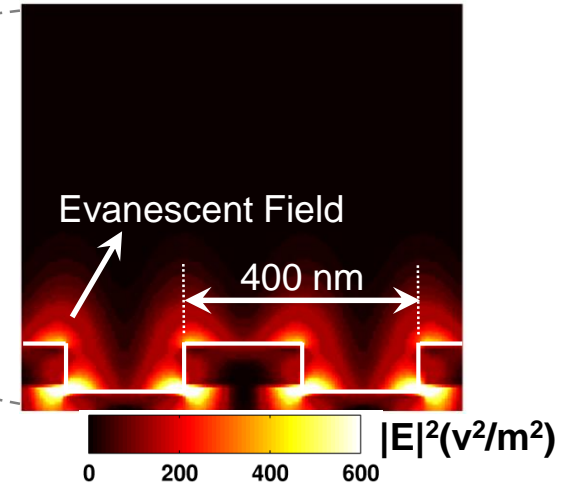
Photonic Crystal Biosensors

DNA Nanotechnology

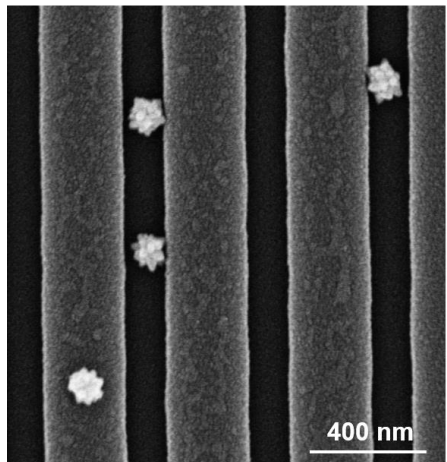
Principle of Photonic Crystal Nanoparticle Sensing



Computer simulation:
Finite-Difference Time-Domain (FDTD)

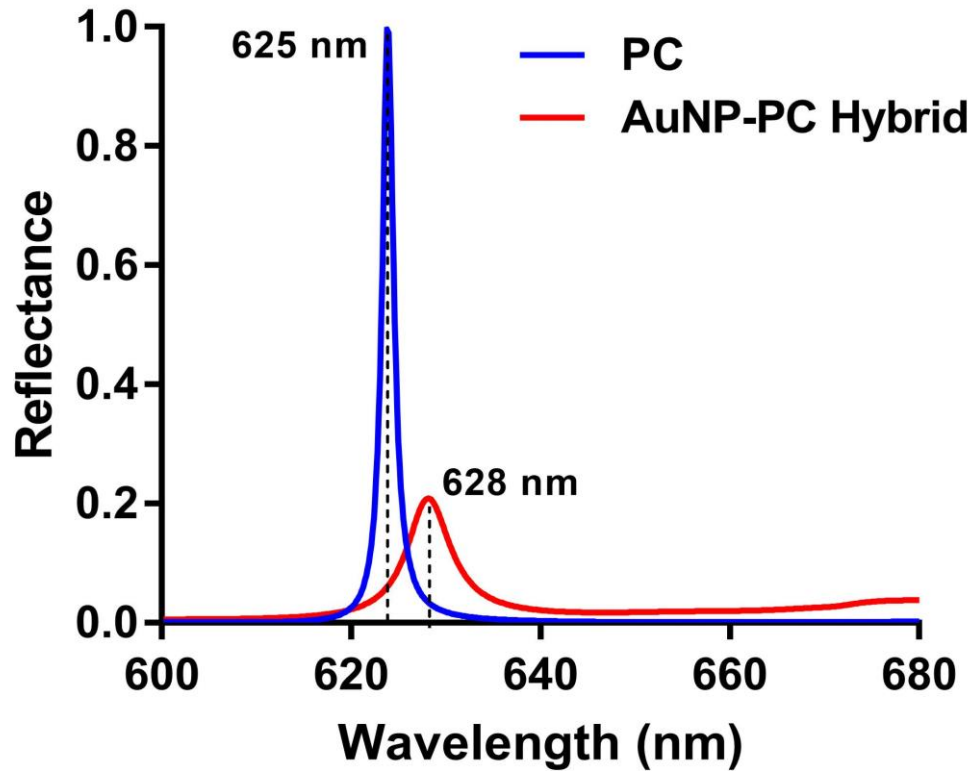


Measure {
Peak Wavelength Value (PWV)
Peak Intensity Value (PIV)

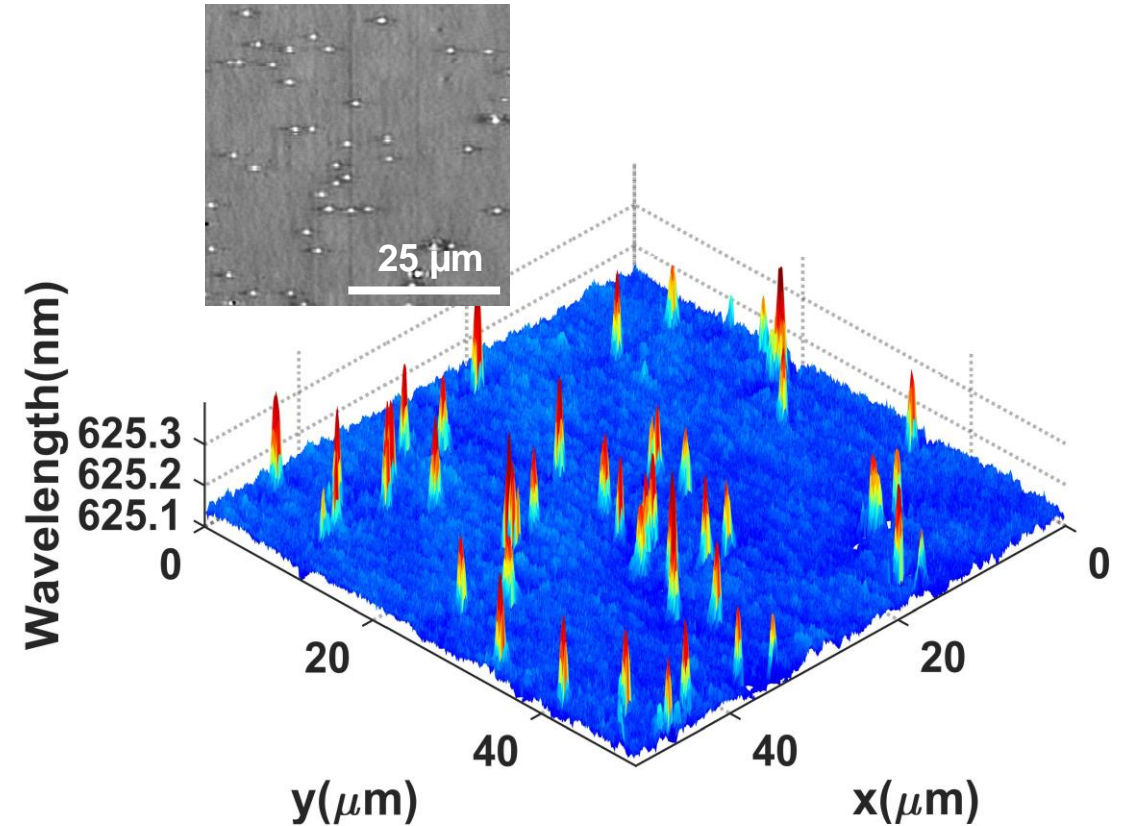


Digital Resolution of AuNP "Tags": Detection Method

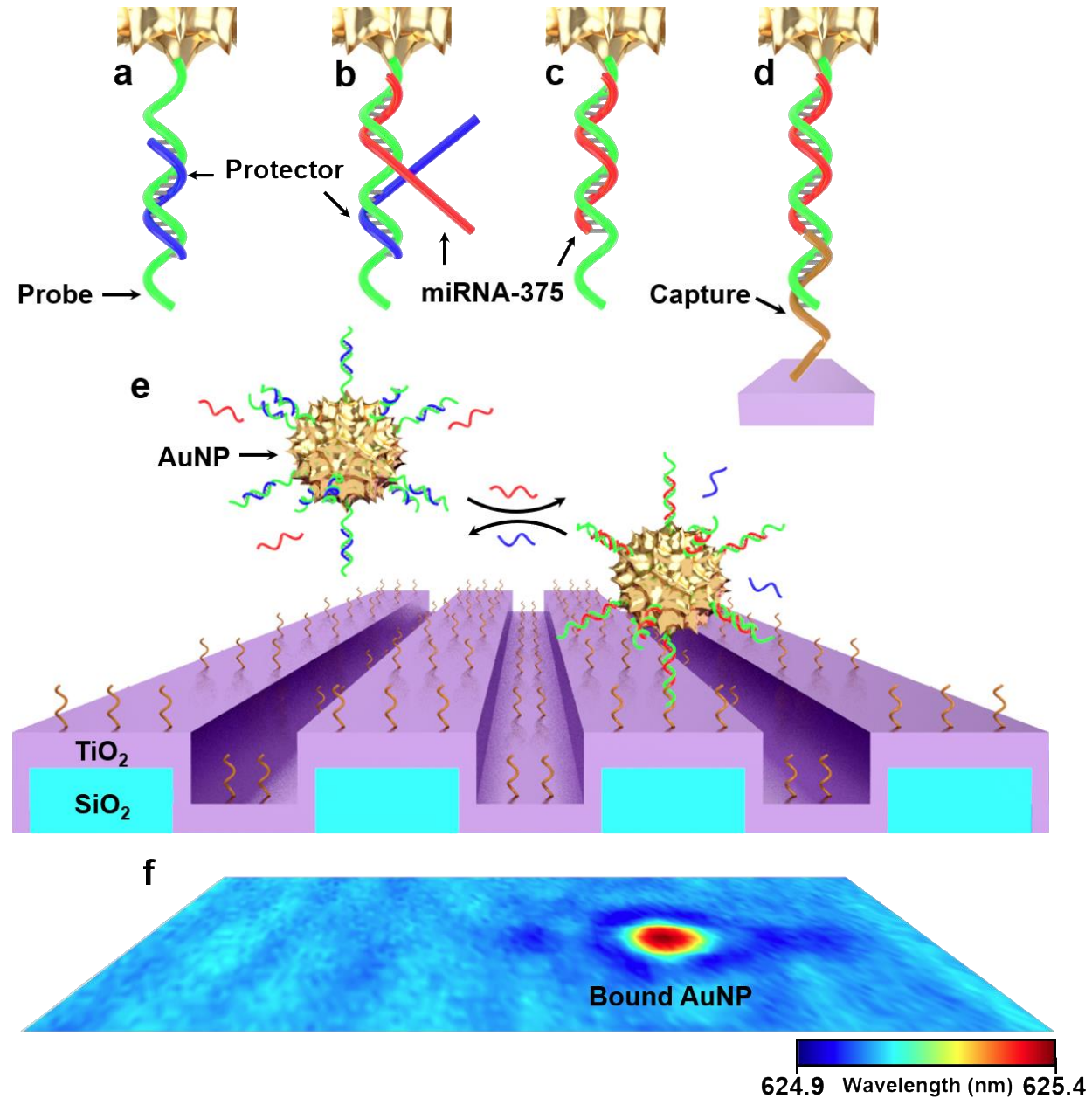
Hybrid causes drop in PC reflectance peak intensity & shift in wavelength



Allows for digital resolution of particles



Active Capture + Digital Counting (AC+DC) miRNA Diagnostics



2 hour endpoint

miR-375 + AuNPs

Canady et al. PNAS, 2019

Background

0.1 fM

1 fM

10 fM

100 fM

1 pM

10 pM

1 min

30 mins

60 mins

90 mins

120 mins

miR-375 + AuNPs

625.0 625.3

25 μ m

Highlights

Photonic Crystal Biosensing: Enhanced E-field @ resonance → nanoparticle detection

Toehold DNA Probes: Optimize hybridization by $\Delta G_{RXN} \cong 0$ → single base selectivity

AC+DC Assay: Combine AuNP-DNA probe (selectivity) & PC biosensors (sensitive) for rapid, no amplification, and no wash miRNA detection

AC+DC Data:

miRNA detection with 10^6 dynamic range (100 aM lowest)

Single base selectivity across 22mer miRNA (5 examples)

Detection in complicated background (excess non-target RNA)

Future: Microfluidic implantation, additional photonic-microscopes