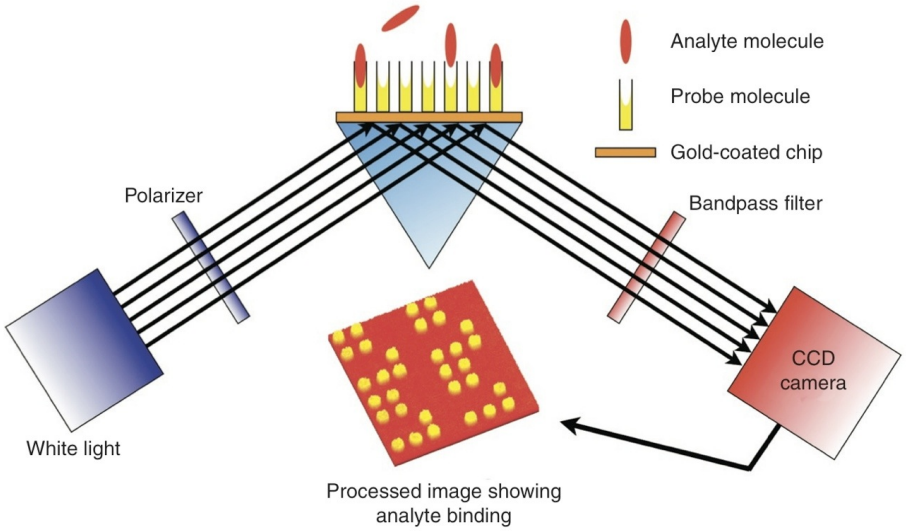
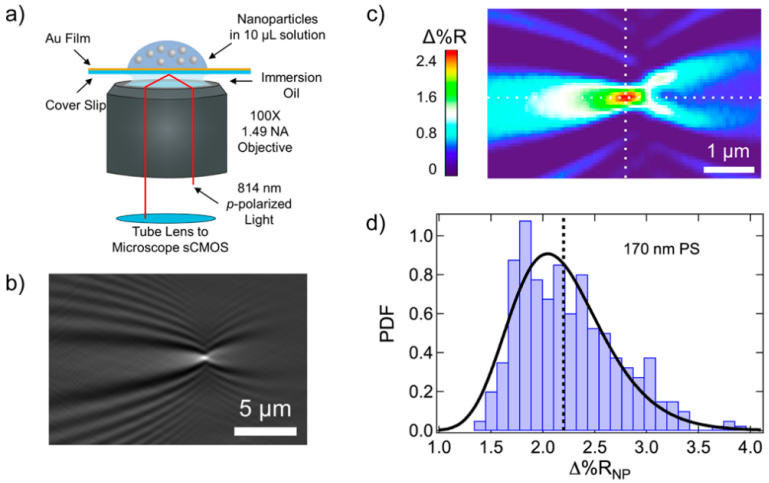
SPR Imaging Measurements of DNA Microarrays and Nanoparticles

Surface Plasmon Resonance Imaging (SPRI) of DNA microarrays

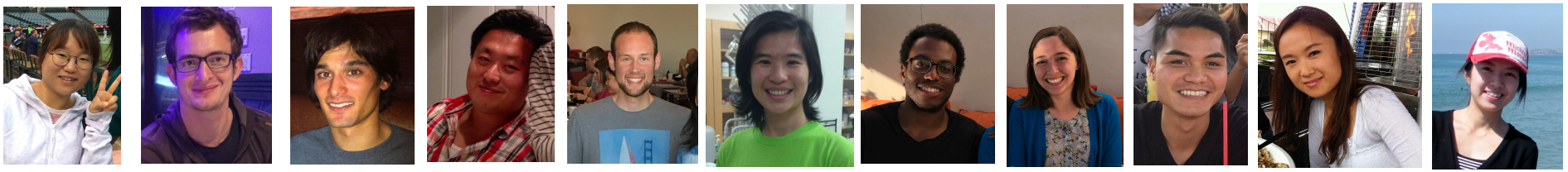


Single Nanoparticle SPRI Microscopy Bioaffinity Uptake



Nanoparticle-Enhanced SPRI of Microarrays

Robert M. Corn - UCI Department of Chemistry



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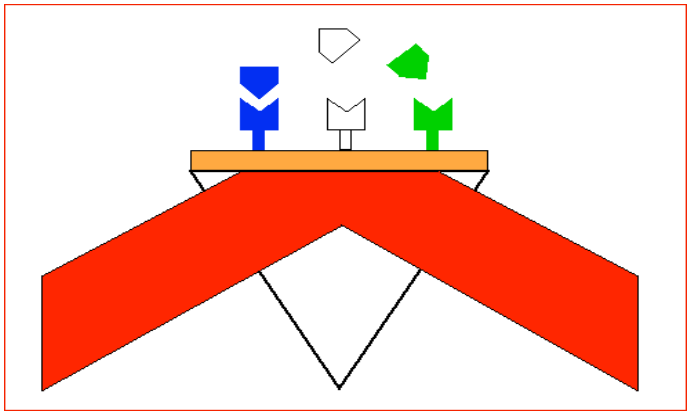
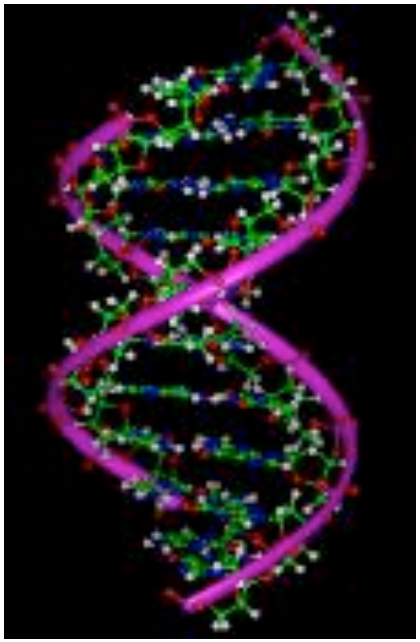
Adsorption Biosensors

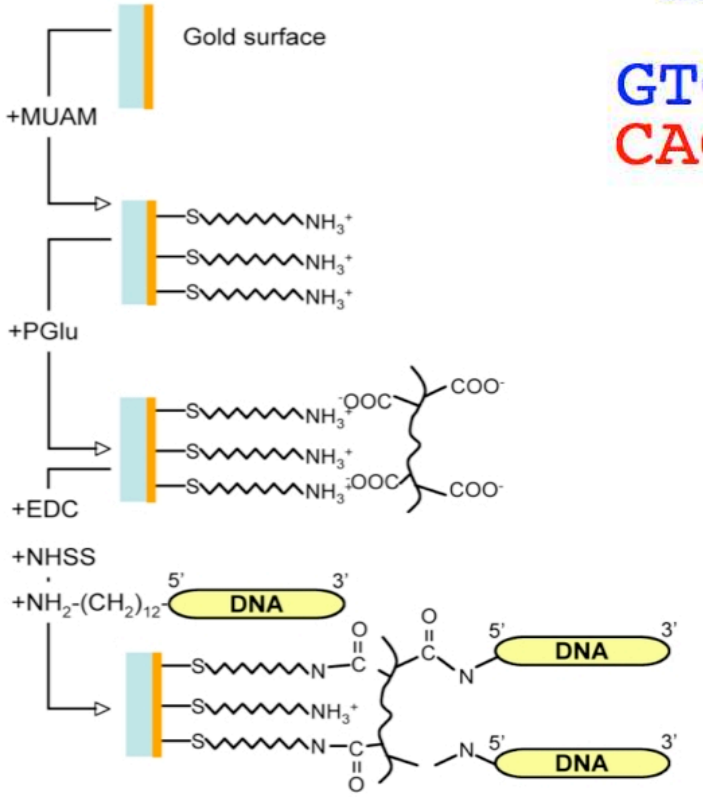




DNA-DNA
Binding

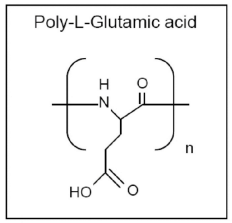
Target molecules (DNA, proteins, biomarkers) are detected when they adsorb to a surface.

Surface Attachment Chemistry: MUAM-pGlu + NHSS/EDC coupling



DNA microarrays

pGlu



Dr. Yulin Chen

Y. Chen et al., *Langmuir*, **25** 5054-5060 (2009).

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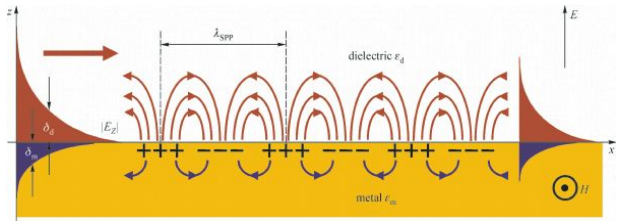
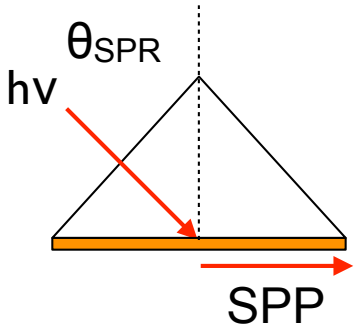
Surface Plasmon Resonance Imaging (SPRI)



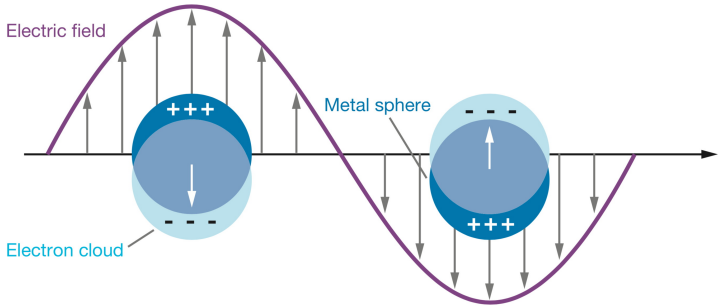
Surface Plasmon Polaritons (SPPs)



Resonant Angle (Momentum) Matching at ANY SPP wavelength

VERSUS

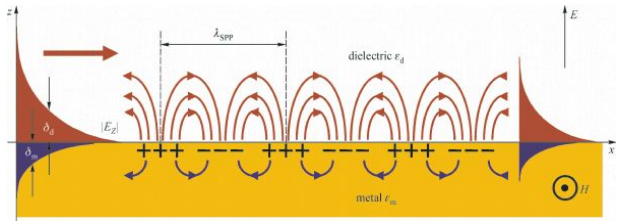
Localized Surface Plasmon Resonance (LSPR)



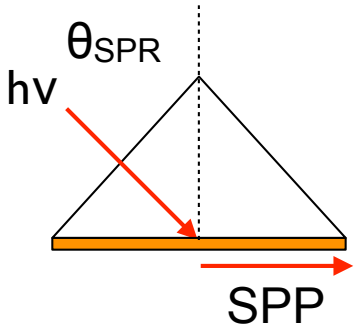
Resonant Optical Absorption Process at ONE wavelength

SPR image: J. Wang, Front. Optoelectron. 7, 320-337 (2014)
LSPR image: K. A. Willets and R. P. Van Duyne, Annu. Rev. Phys. Chem., 58, 267-297 (2007).

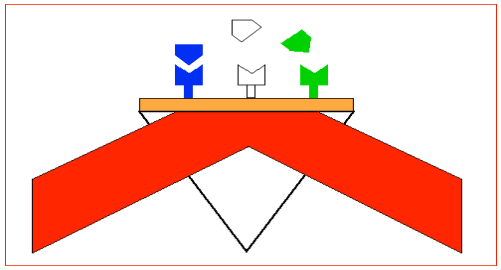
Surface Plasmon Resonance Imaging (SPRI)

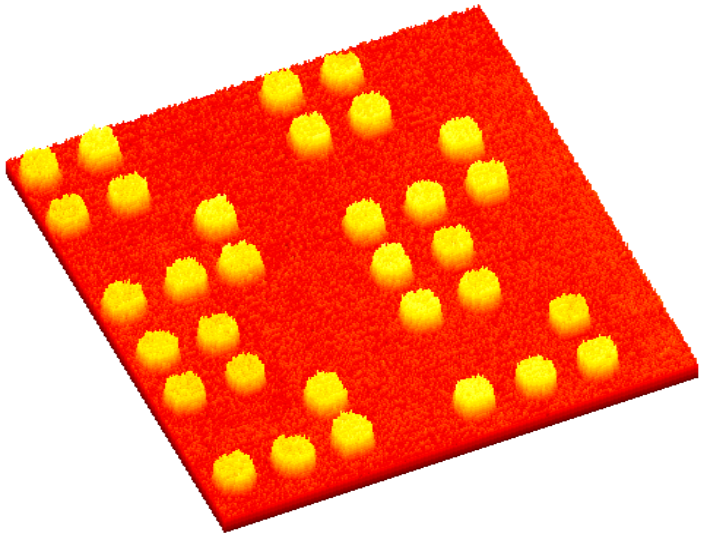


Surface Plasmon Polaritons (SPPs)



SPRI is a multiplexed surface microarray biosensing format





Array Format = Best Biosensing!

SPR image: J. Wang, Front. Optoelectron. 7, 320-337 (2014)
LSPR image: K. A. Willets and R.P. Van Duyne, Annu. Rev. Phys. Chem., 58, 267-297 (2007).

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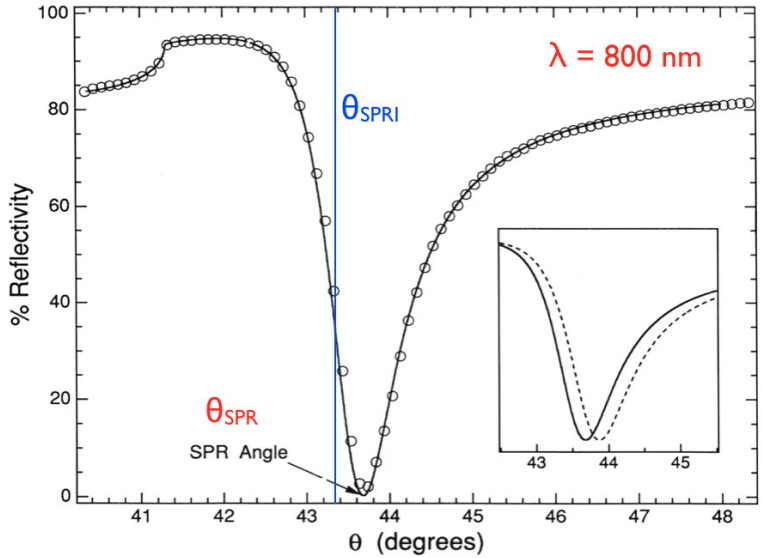
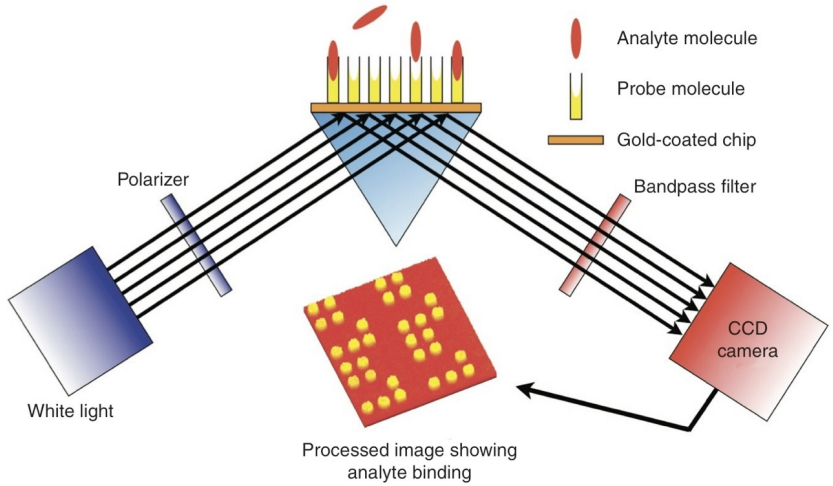
Surface Plasmon Resonance Imaging (SPRI)

SPRI angle



SPR Imaging



SPR imaging or microscopy measures the change in reflectivity at the SPRI angle.
A differential SPRI image shows the changes upon adsorption for an entire surface or microarray.

- *SPRI measurements can be made at all wavelengths above the SPP cutoff wavelength (540 nm for gold). We choose 800 nm for SPRI measurements on gold thin films (45 nm).*
- *SPPs propagate on the gold thin film typically for tens of microns, and extend (decay exponentially) 200 nm into solution.*

*B. Rothenäusler and W. Knoll, Nature **332**, 615-617 (1988).*
*JM Brockman, BP Nelson and RM Corn, Ann. Rev. Phys. Chem., **51** 41-63 (2000).*

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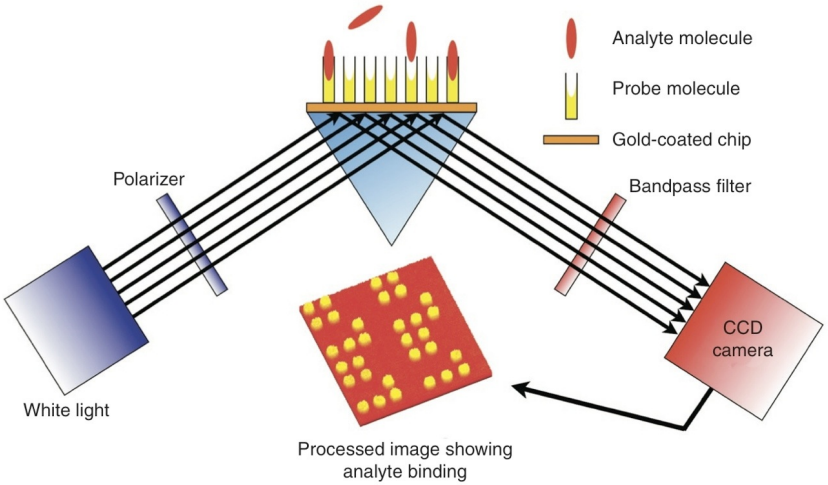
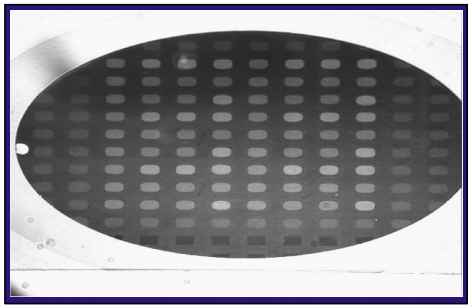
Surface Plasmon Resonance Imaging of Biosensor Arrays





Prof. Hye Jin Lee, KNU

In SPRI, bioaffinity adsorption changes the local interfacial refractive index which leads to an increase in reflectivity - Δ%R.

Bioaffinity sensing with SPRI is now a well-established field around the world, with commercially available instrumentation (e.g., Horiba, IBIS) and many new exciting extensions and applications.

Extreme Biosensing: Dec. 2018
Kauai, Hawaii.

Surface Plasmon Resonance Imaging: What Next?
G. Spoto and M. Minunni J. Phys. Chem. Lett., ***3****, 2682–2691 (2012).*

Reviews: S. Scarano et al., Biosensors and Bioelectronics ***25****, 957-966 (2010).*
J. B. Fasoli and R. M. Corn, Langmuir, ***31*** *9527-9536 (2015).*

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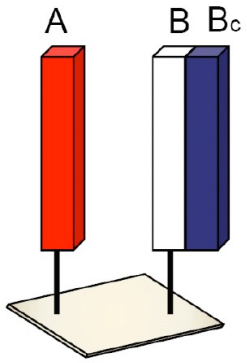
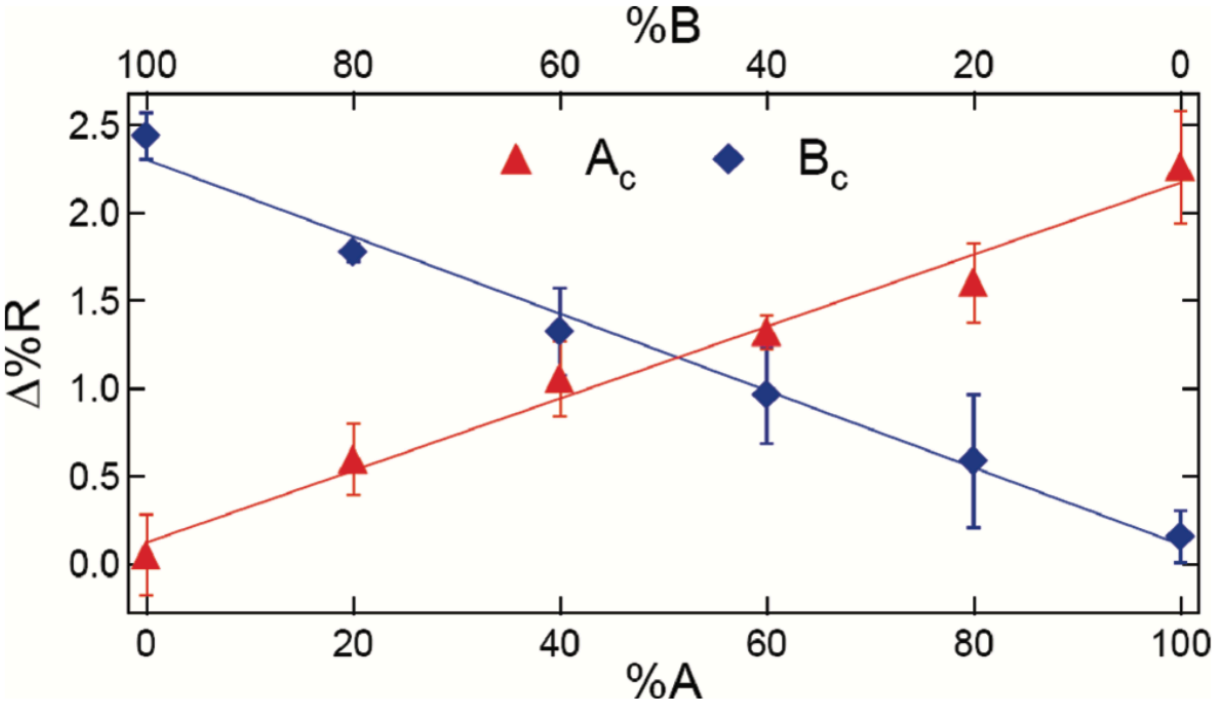
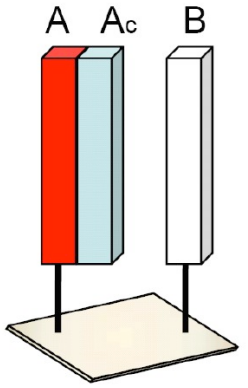
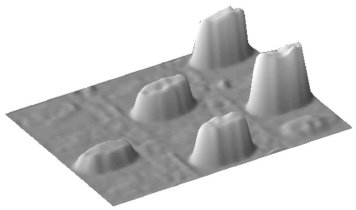
SPRI measurements of DNA microarrays: Quantitative Surface Chemistry!

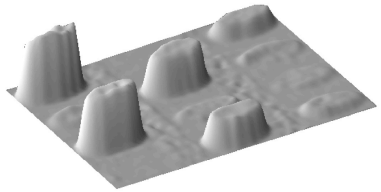
DNA Hybridization Adsorption on Binary (A/B) Mixed Monolayers











Quantitative Mixed Monolayer Measurements

Y. Chen et al., *Langmuir*, **25** 5054-5060 (2009).

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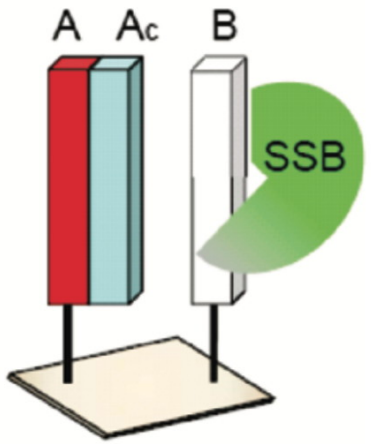
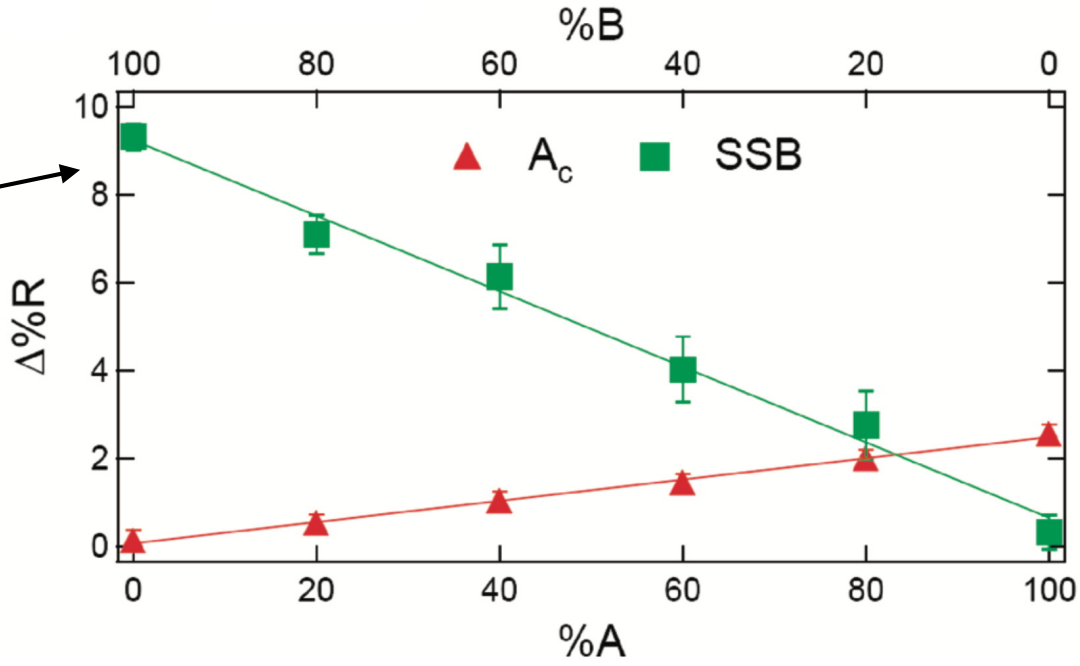
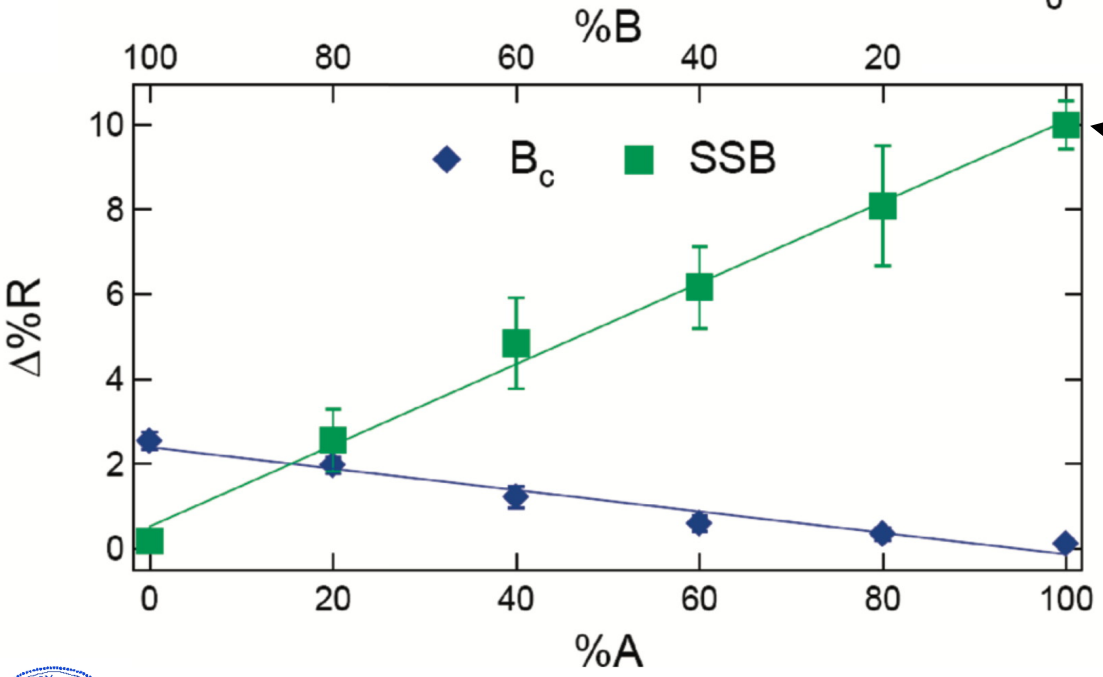
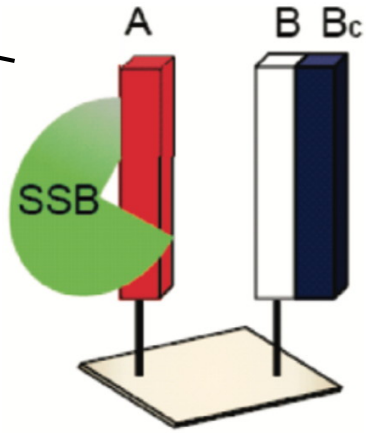
Single Strand Binding Protein (SSB) Adsorption

Protein Biosensing









Y. Chen et al., *Langmuir*, **25** 5054-5060 (2009).

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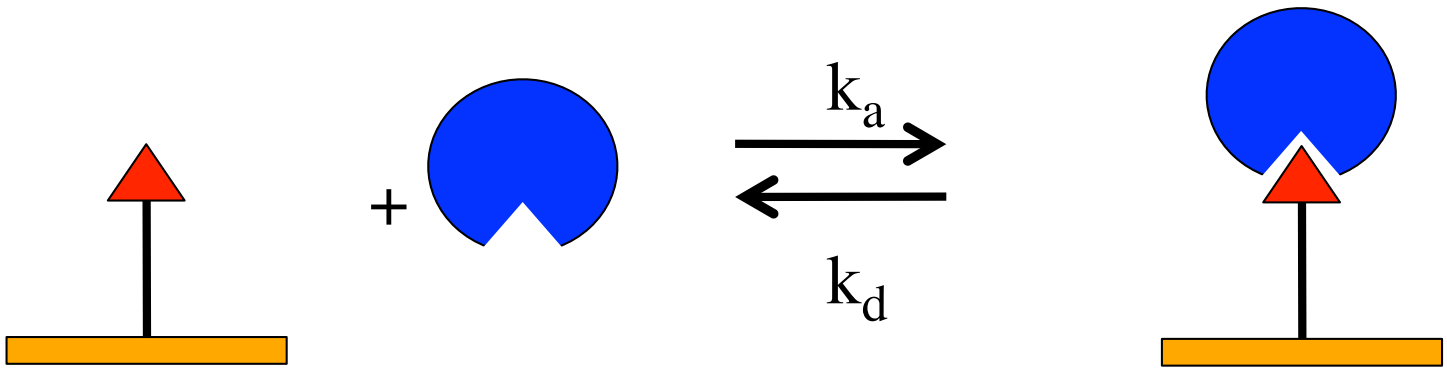
Real-time SPRI for Quantitative Langmuir Adsorption Kinetics and K_{ads}

S15: Lys-Glu-Thr-Ala-Ala-Ala-Lys-Phe-Glu-Arg-Gln-His-Met-Asp-Ser

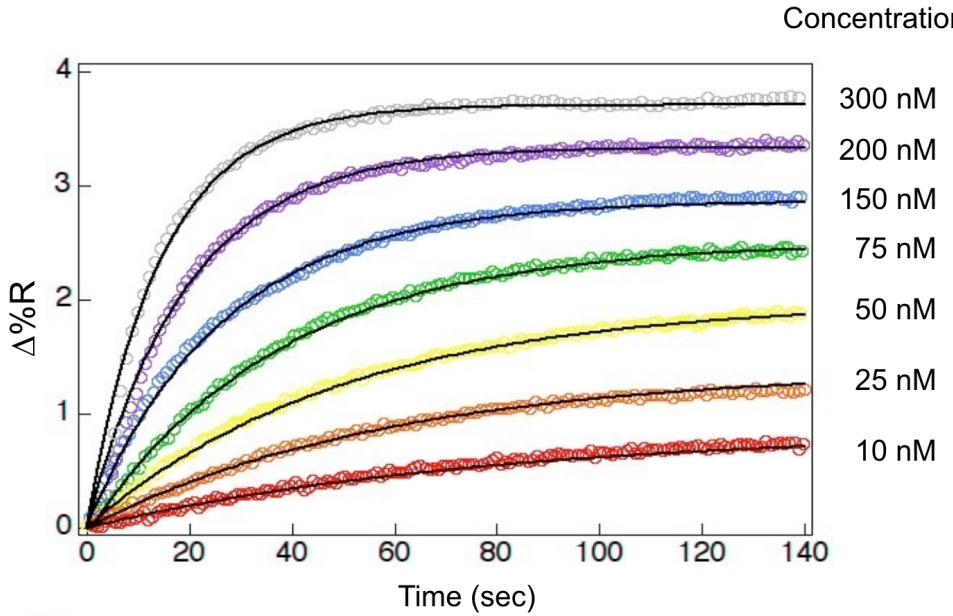


$$K_{ads} = \frac{k_a}{k_d}$$

$$\theta = \Gamma/\Gamma_{tot}$$

S protein - S15 peptide

$$\theta(t) = \theta^{eq}\left(1 - \exp(-(k_a C + k_d)t)\right)$$



$k_a = 1.9 \times 10^5\ M^{-1}\ s^{-1}$

$k_d = 1.1 \times 10^{-2}\ s^{-1}$

$K_{ads} = 1.7 \times 10^7\ M^{-1}$

$$K_{ads} = \frac{\theta_{eq}}{C(1 - \theta_{eq})}$$

Greta Wegner

G. J. Wegner et al. Analytical Chem., 76 5667-5684 (2004).

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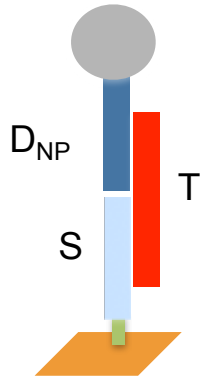
Nanoparticle-Enhanced SPRI

DNA-functionalized:

- Silica Nanoparticles
- Polystyrene Nanoparticles
- Gold Nanoparticles*



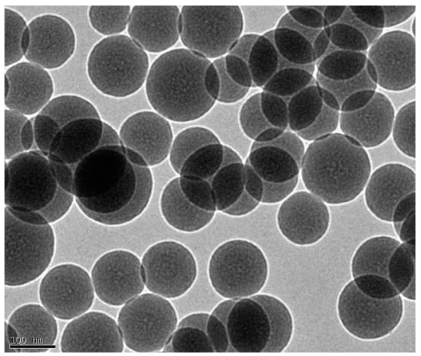
Dr. WenJuan Zhou

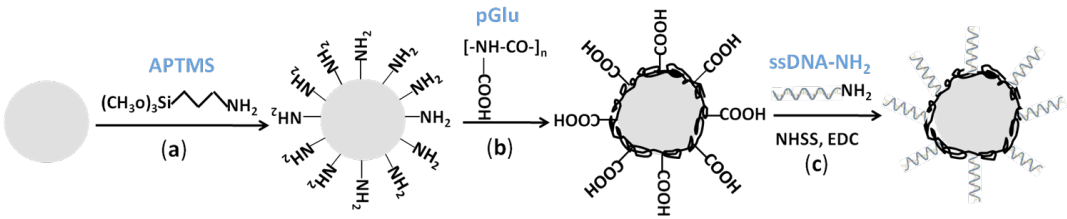
Three sequence hybridization assay with SPR-PI

*Nanoparticle-Enhanced SPRI with AuNPs first used by L. He et al., JACS 38 9017-9077 (2000)

pGlu DNA Attachment Chemistry on Silica Nanoparticles (SiNPs)

TEM





100 nm silica nanoparticles (SiNPs)

W. J. Zhou et al., Analytical Chemistry, **83** 3897-3902 (2011).

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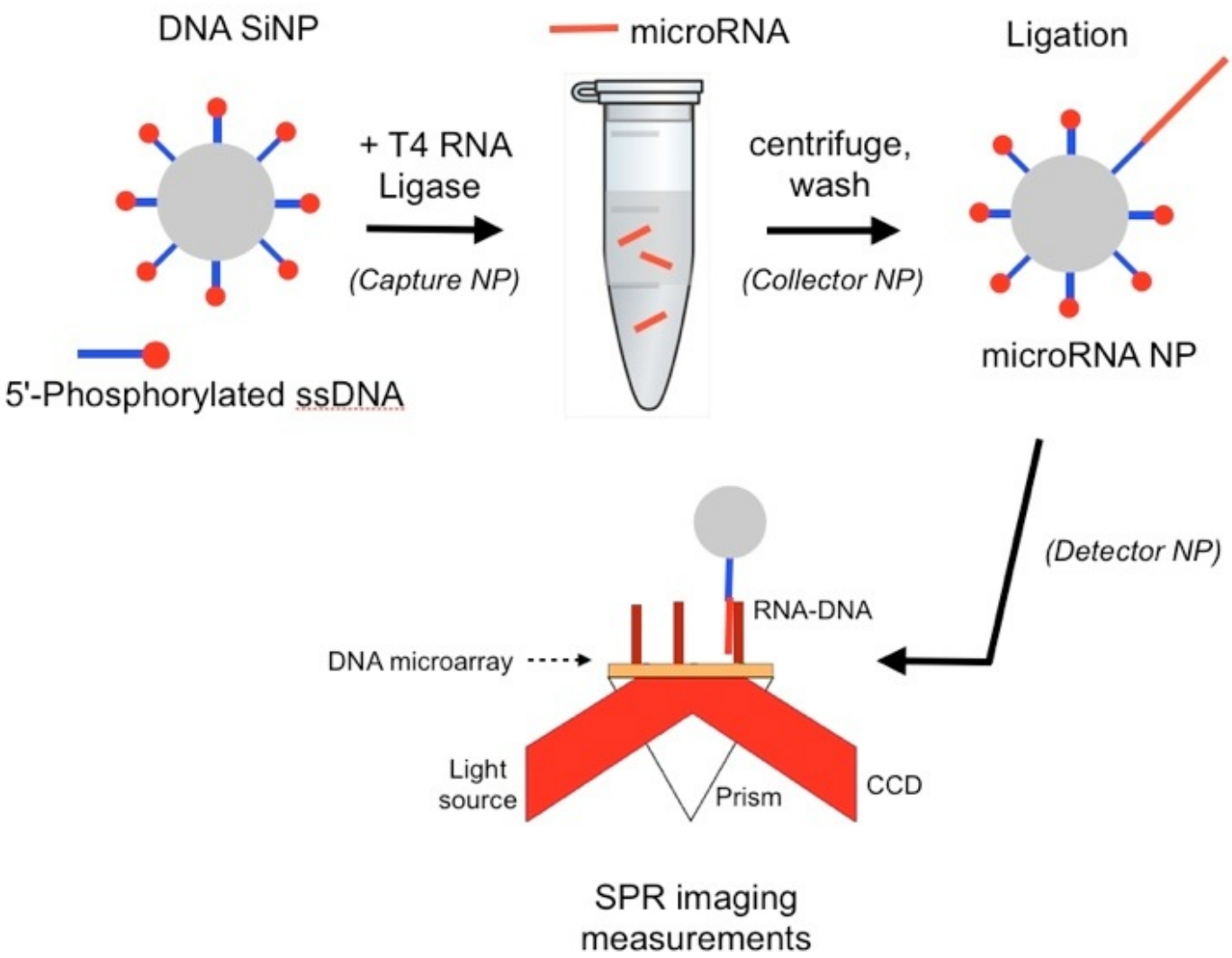
Surface Enzyme Chemistry + Nanoparticle-Enhanced SPRI

- *MicroRNA Detection with Enzymatic Nanoparticles: Ligation Capture*



Dr. Yulin Chen

Dr. WenJuan Zhou

T4 RNA Ligation for miRNA capture

*W. J. Zhou et al., Analytical Chemistry, **83** 3897-3902 (2011).*

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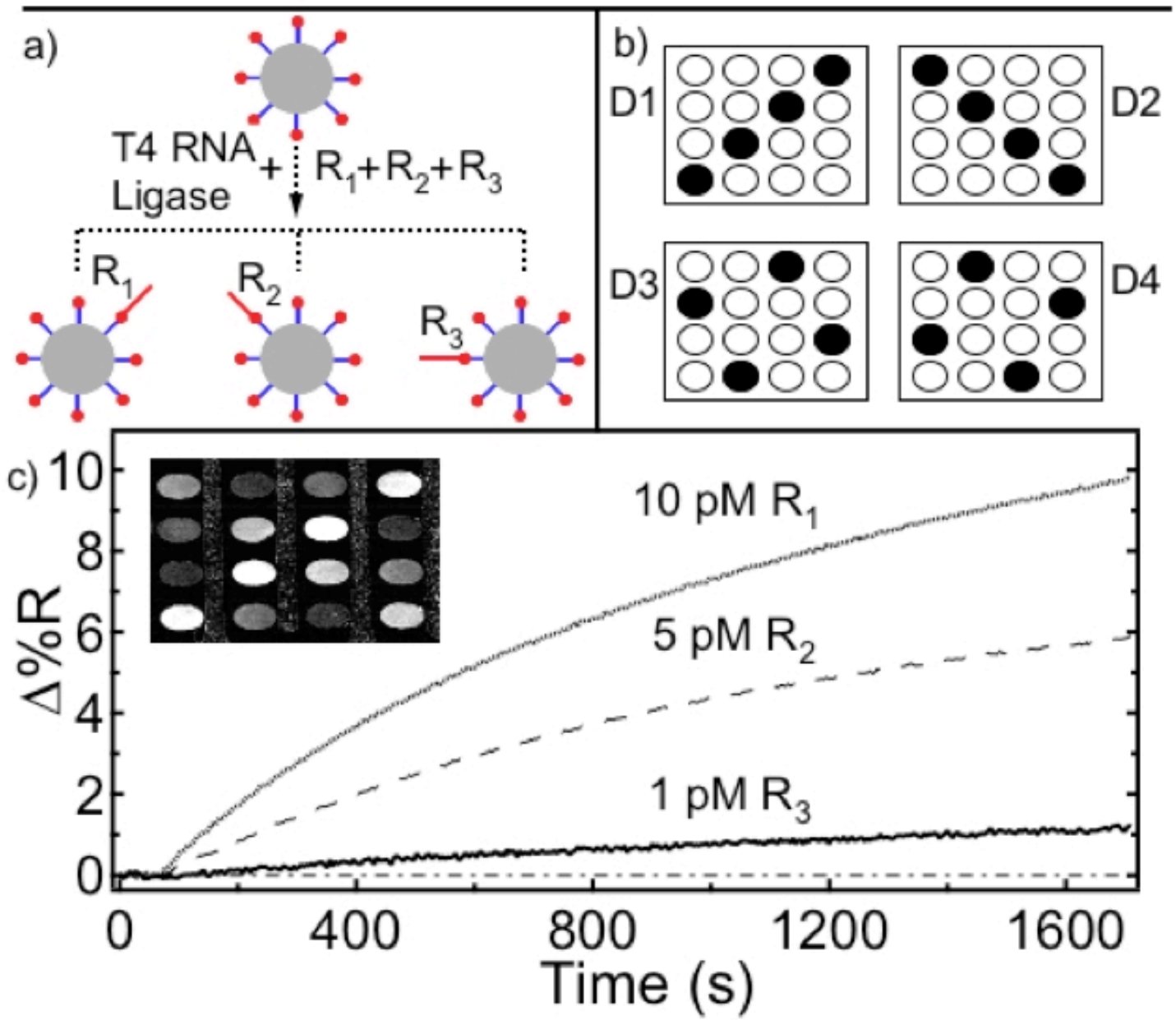
MicroRNA Detection with Enzymatic Ligation Capture Nanoparticles



Multiplex Detection!

W. J. Zhou et al., *Analytical Chemistry*, **83** 3897-3902 (2011).

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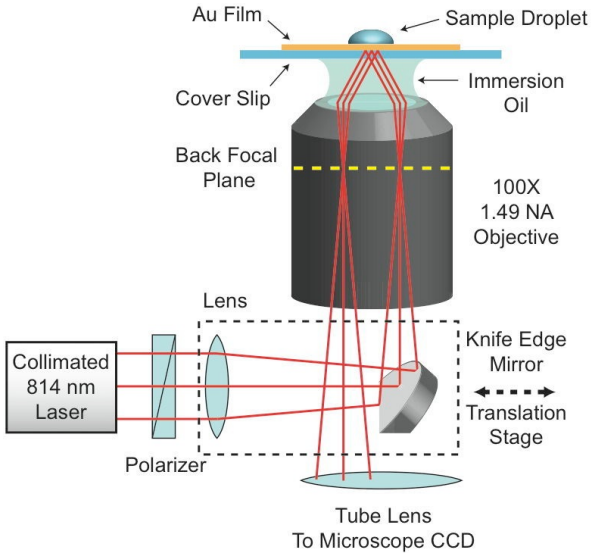
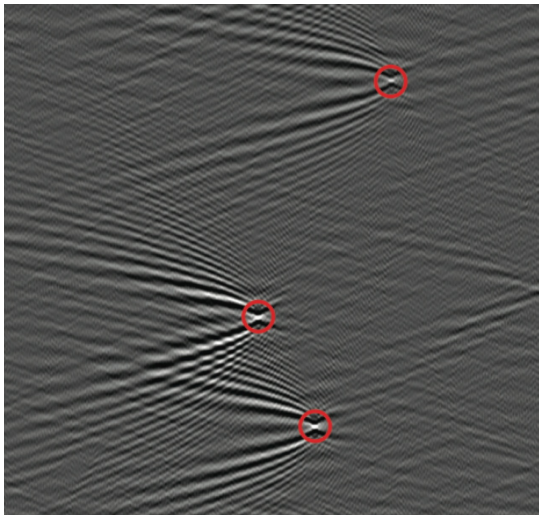
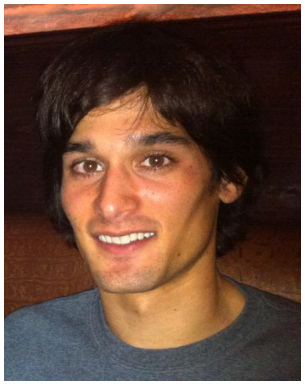
Single Nanoparticle SPR Imaging Microscopy

Single Nanoparticle SPRI Uses Traveling Wave Surface Plasmon Polaritons!







Aaron Halpern

Adam Maley

Brandon Matthews

Mike Cho

Corn Group Website

https://rmcorninfo.weebly.com/

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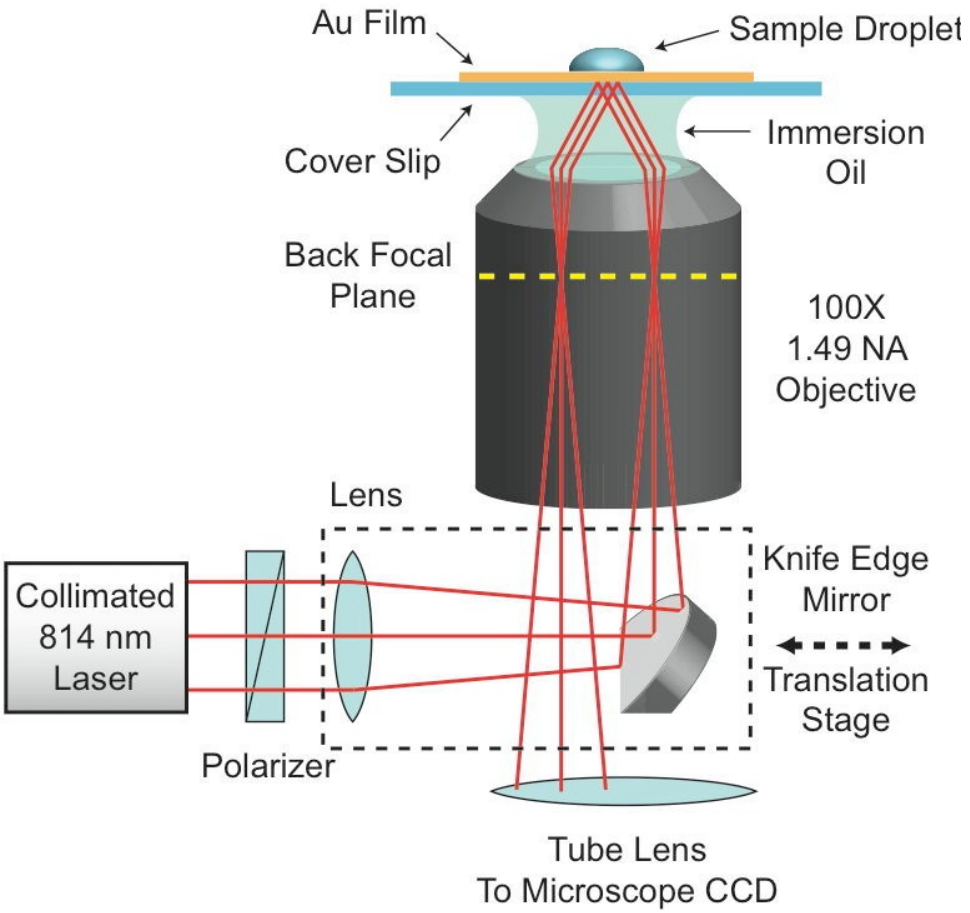
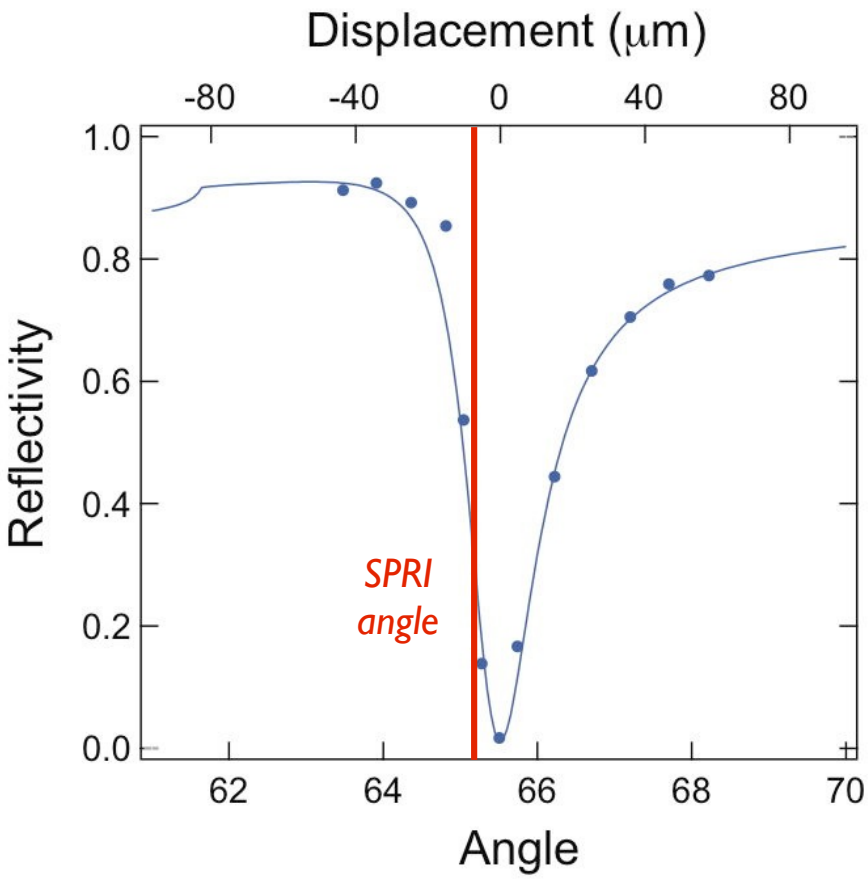
Near Infrared TIR SPR microscope: 814 nm





100x Objective
N.A. = 1.49
90 *μm* x 70 *μm* FOV

Control angle of incidence by varying d

A. R. Halpern, J. B. Wood, Y. Wang and R. M. Corn, ACS Nano, ***8*** *1022-1030 (2014).*

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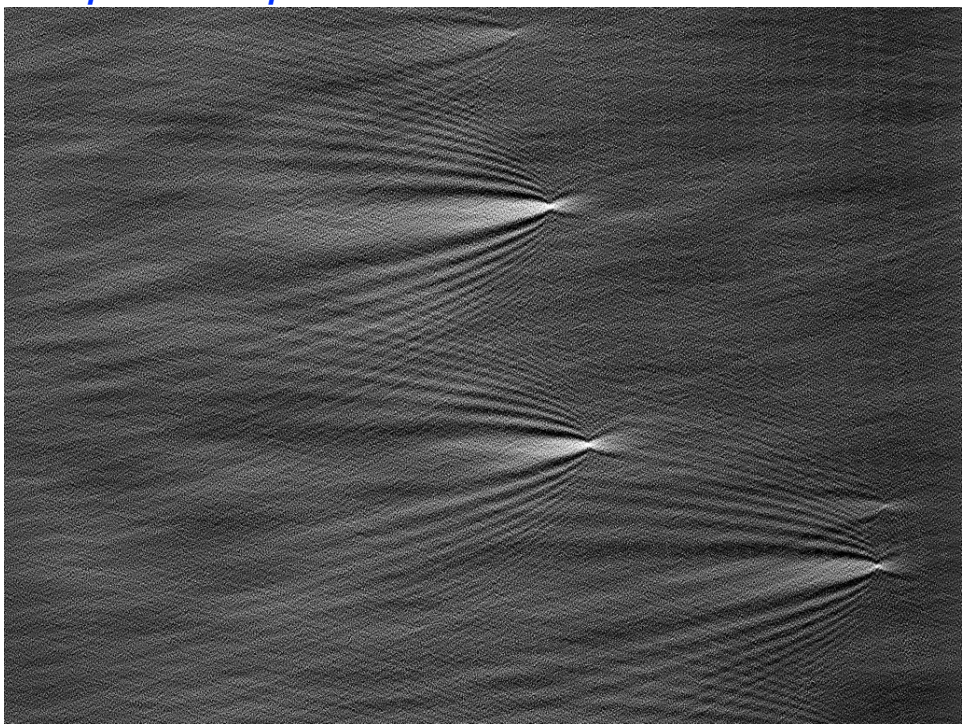
Near Infrared TIR SPRI microscope data: irreversible NP adsorption

90 μm x 70 μm FOV *40 nm AuNPs*

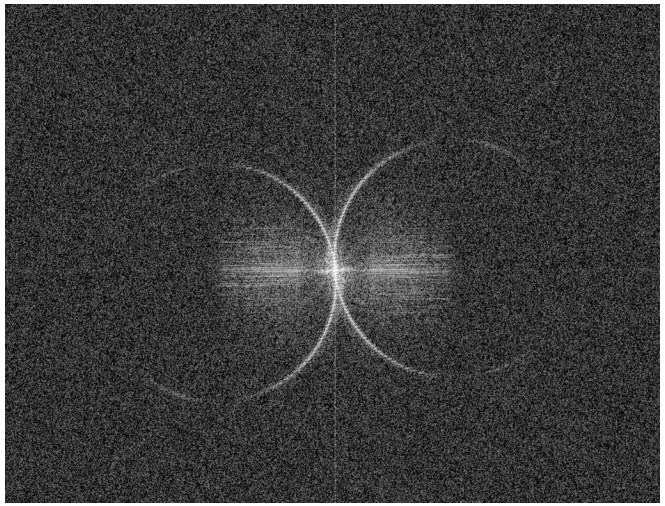


3 second SPRI differential reflectivity image

Each adsorbed nanoparticle creates a diffraction pattern.

All types of nanoparticles (Au, PS, Hydrogel) create similar diffraction patterns.

2D FFT



Shape and size of the diffraction pattern due to the SPP wavevector (k_{sp}) at 814 nm

$$(\nabla^2 + k_{sp}^2)u(x,y) = 0$$

$$(-\omega_x^2 + -\omega_y^2 + k_{sp}^2)u(\omega_x,\omega_y) = 0$$

Helmholtz Equation Model

$$\omega_x^2 + \omega_y^2 = k_{sp}^2$$

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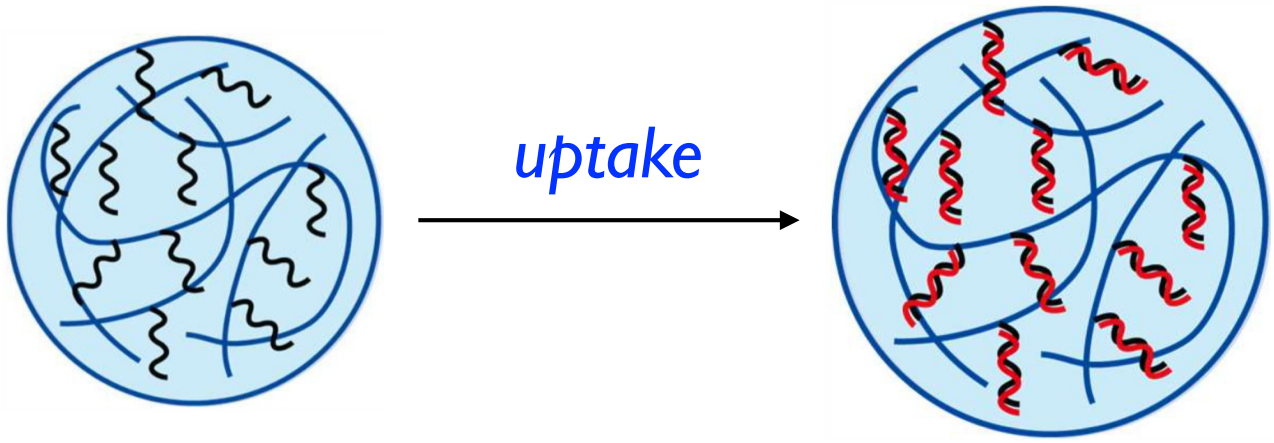
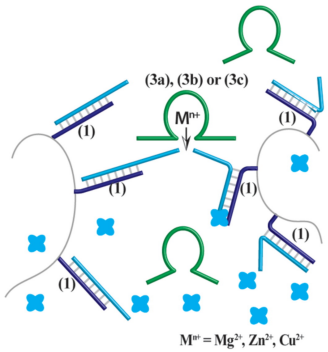
Bioaffinity Uptake in Hydrogel Nanoparticles



Cargo:
DNA and RNA
Aptamers
Proteins
Enzymes
Drug molecules

DNA Hydrogel Nanoparticles for Bioaffinity Transport and Release

Release Mechanisms:
Displacement Reaction
Nuclease Digestion
DNAzyme dissolution



*DNAzyme hydrogel dissolution**

* *S. Lilienthal, Z. Shpilt, F. Wang, R. Orbach, I. Willner, ACS Appl. Mater. Interfaces* **7**, *8923-8931 (2015).*

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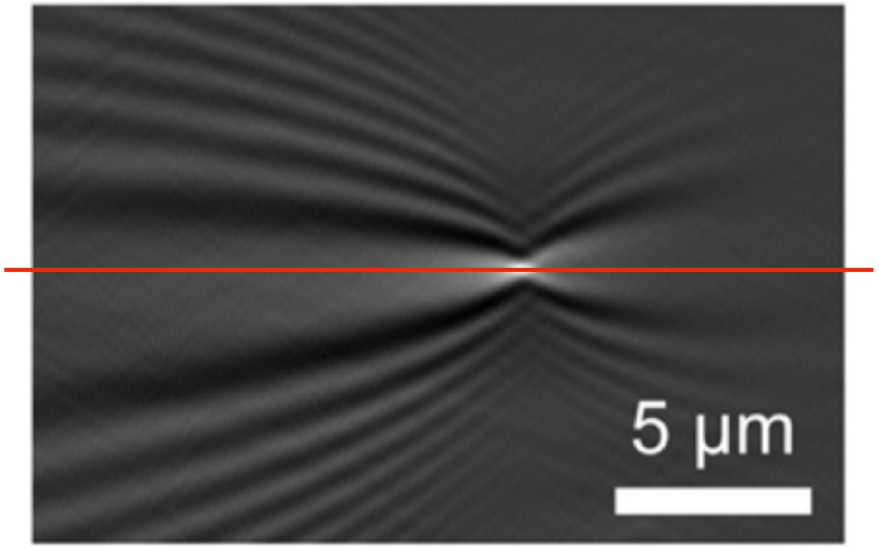
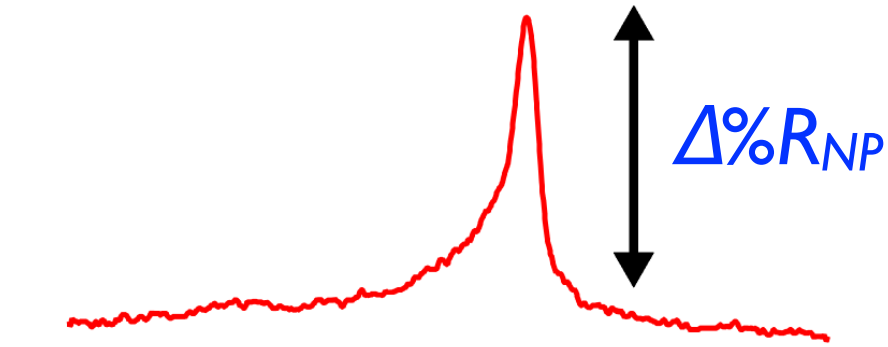
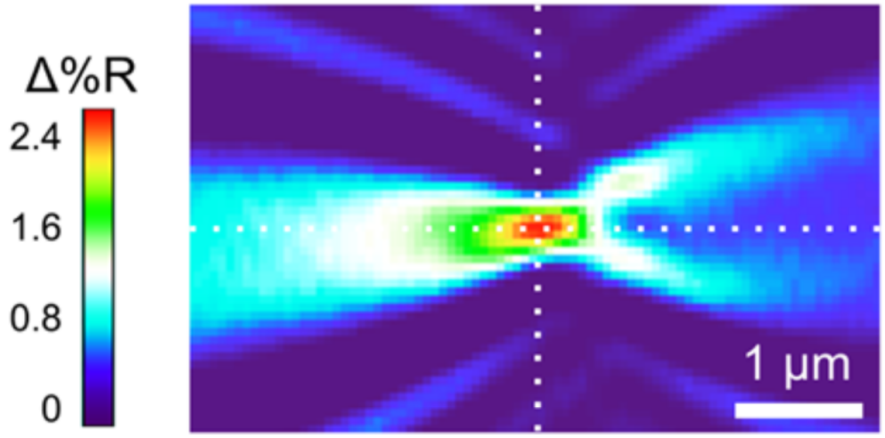
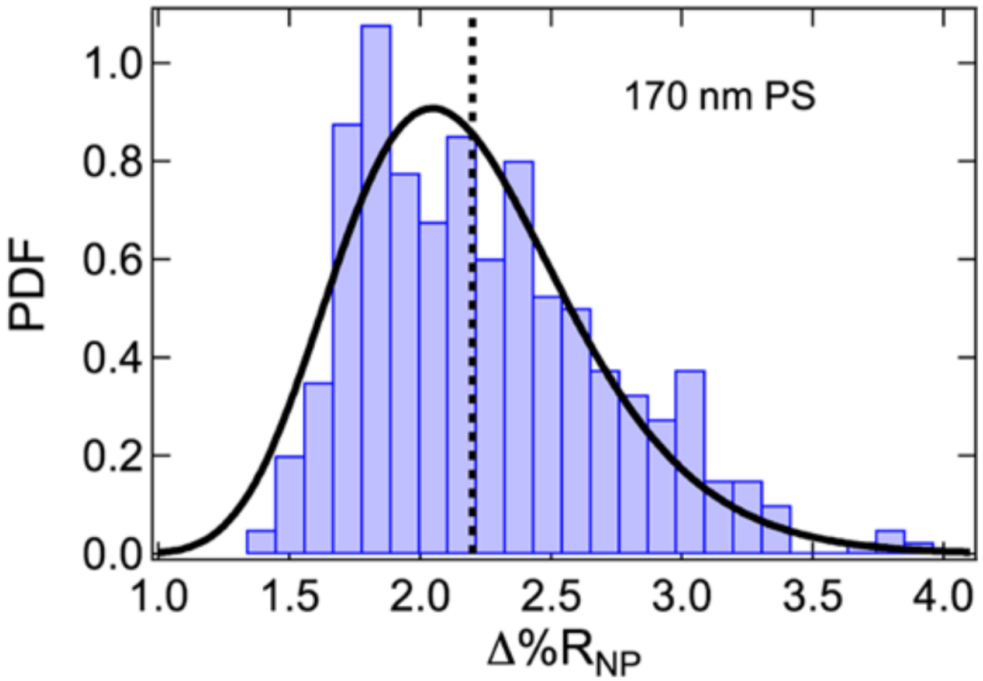
Single Nanoparticle Distribution Measurements





Δ%R_NP "Single Nanoparticle SPRI Reflectivity Change"





A.M. Maley, G.J. Lu, M.G. Shapiro and R.M. Corn, ACS Nano, **11** 7447-7456 (2017).

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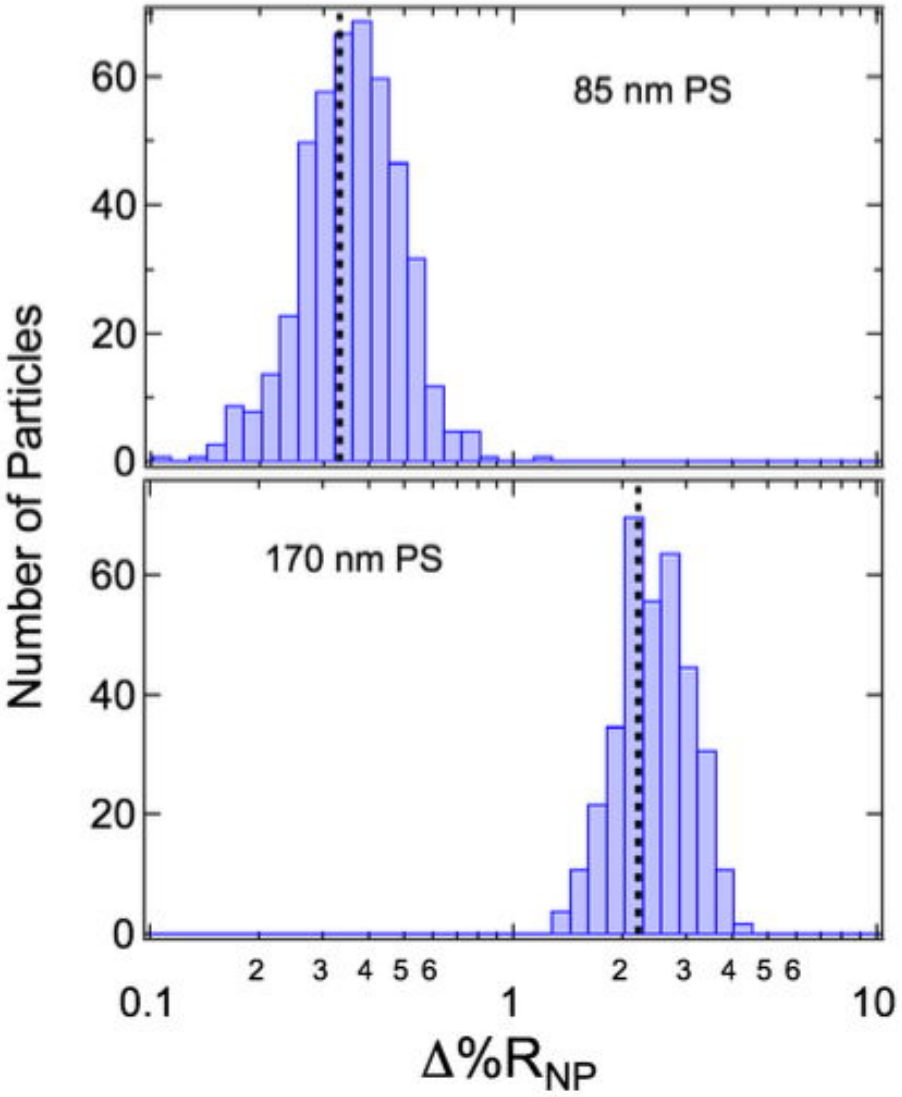
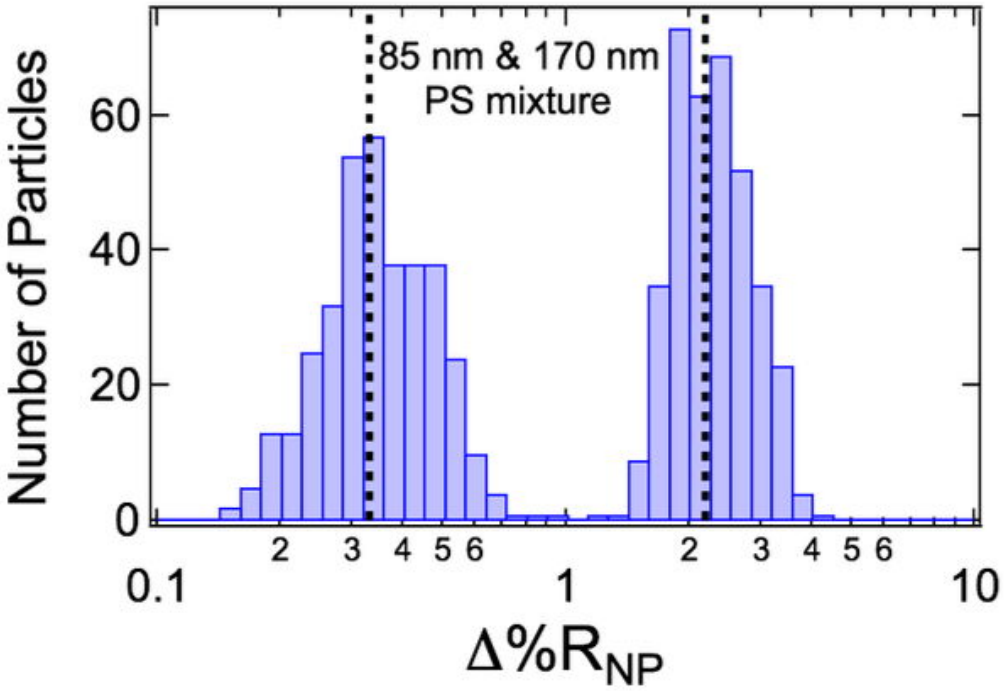
Single Nanoparticle Distribution Measurements



Mixture of Two Polystyrene NPs



A.M. Maley, G.J. Lu, M.G. Shapiro and R.M. Corn, ACS Nano, ***11*** *7447-7456 (2017).*

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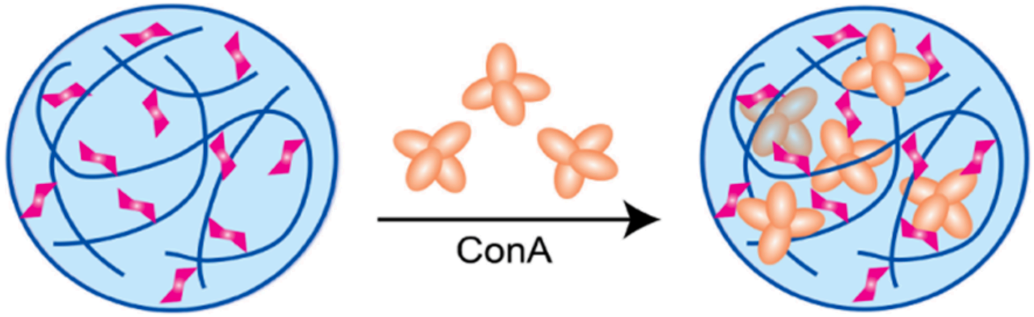
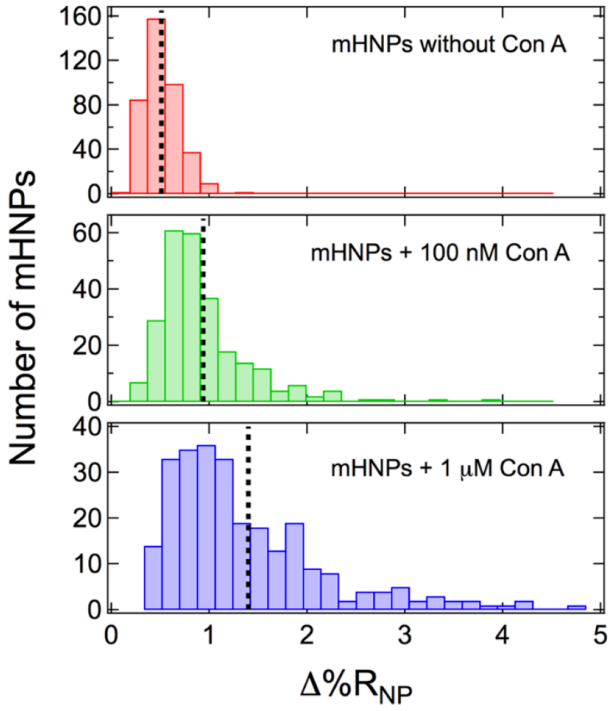
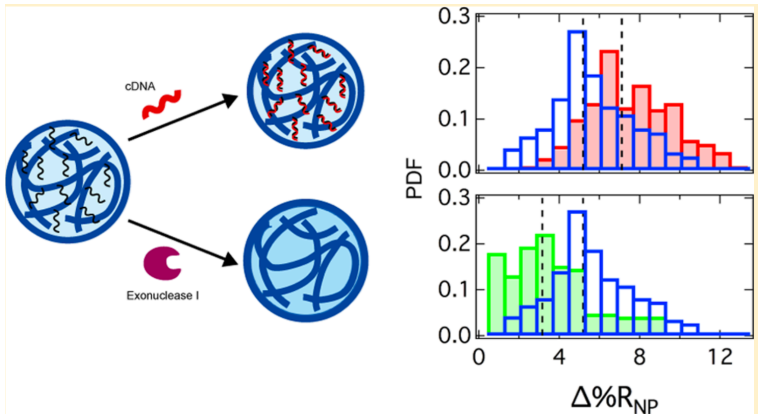
Single Nanoparticle SPRI of Bioaffinity Uptake and Release in Hydrogel NPs



ConA uptake into Mannose-modified Hydrogel Nanoparticles



DNA Hybridization Absorption Exonuclease Release into DNA-modified Hydrogel NPs



A. M. Maley et al., J. Phys. Chem. C, **120** 16843-16849 (2016).

B.M. Matthews et al., J. Phys. Chem. C, **123** 6090-6096 (2019).

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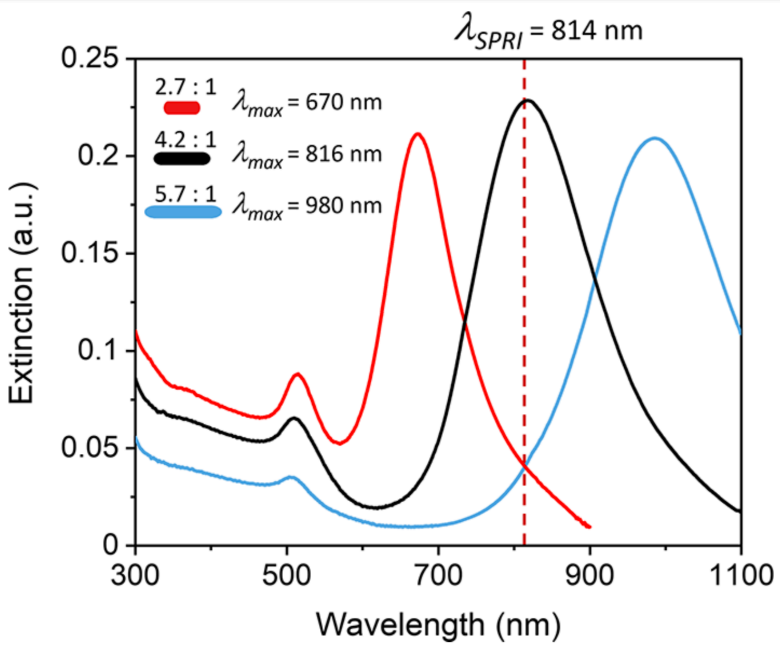
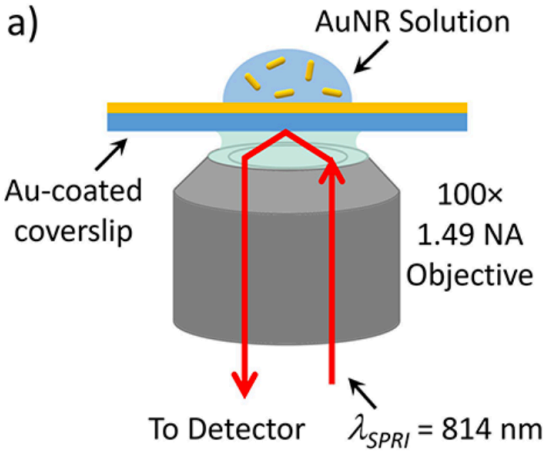
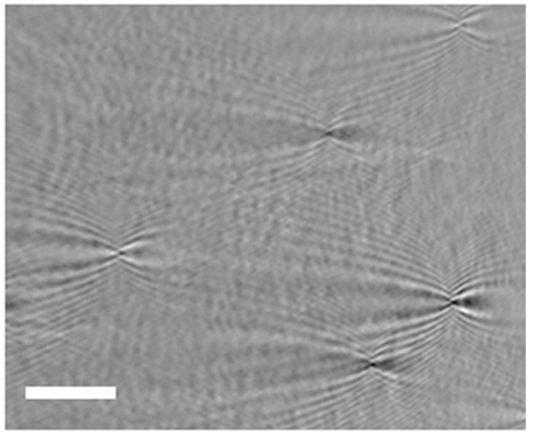
Single Nanoparticle SPRI of Gold Nanorods

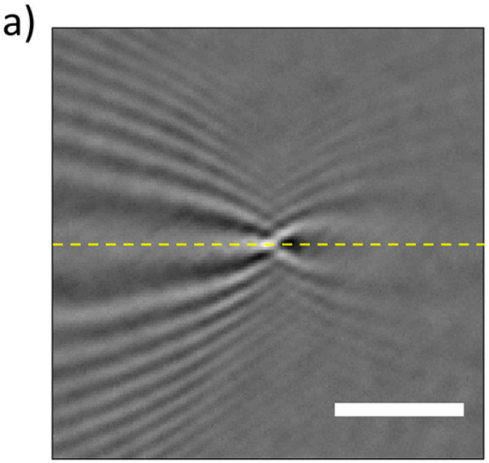


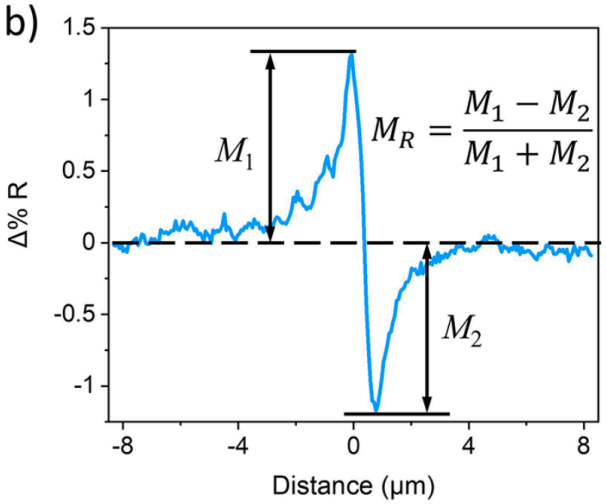




Three AuNR samples: 670, 816, 980 nm

Nonresonant SPRI Resonant LSPR





Yunshan Fan et al. J. Chem. Phys. Lett., **12** 2004-2010 (2021).

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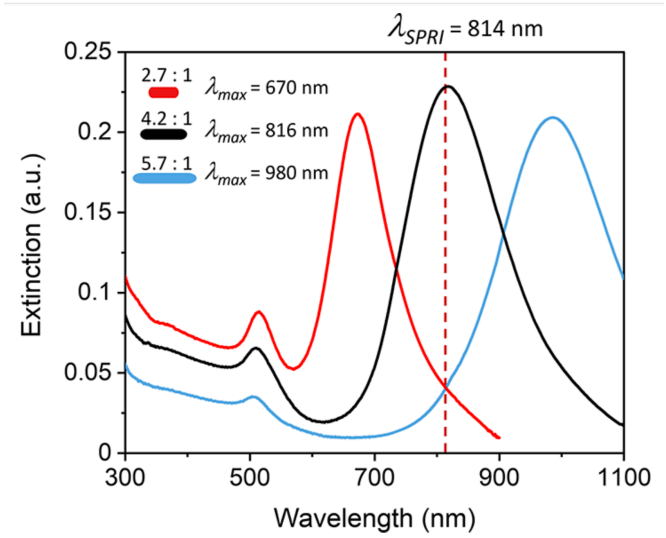
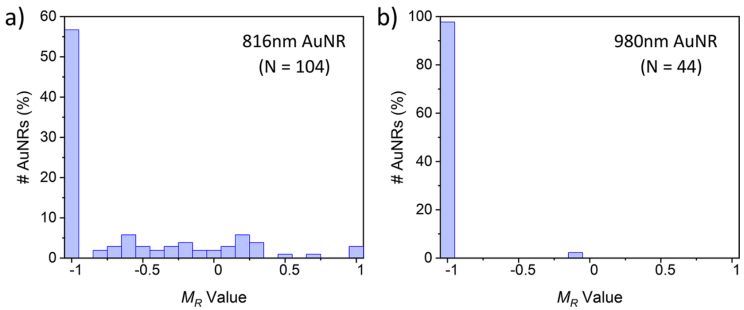
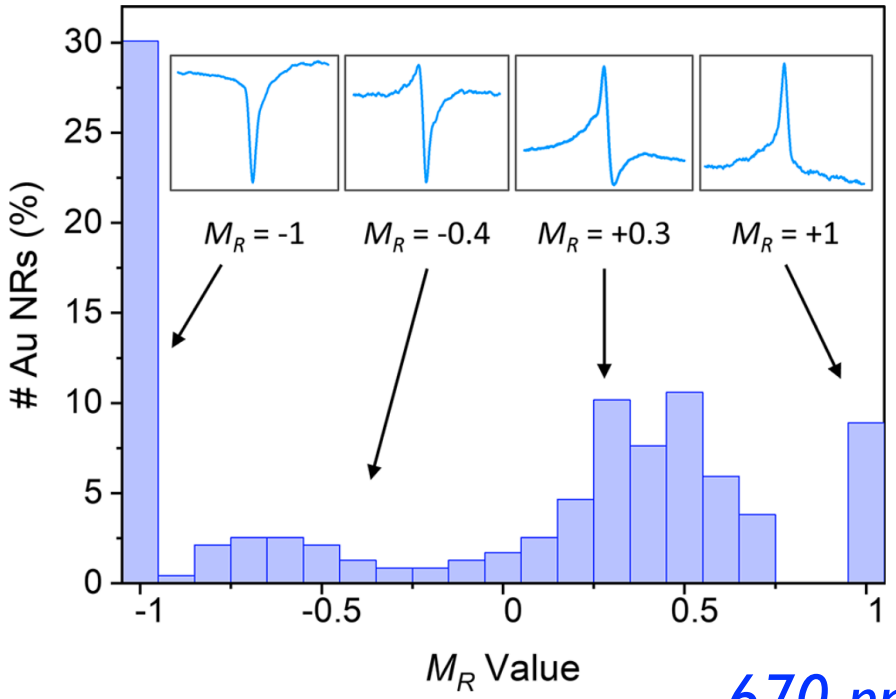
Single Nanoparticle SPRI of Gold Nanorods







670 nm AuNRs

Variations in M_R due to relative positions of SPRI and LSPR wavelengths for individual AuNRs - esp. in the anomalous RI region

Yunshan Fan et al. J. Chem. Phys. Lett., **12** 2004-2010 (2021).

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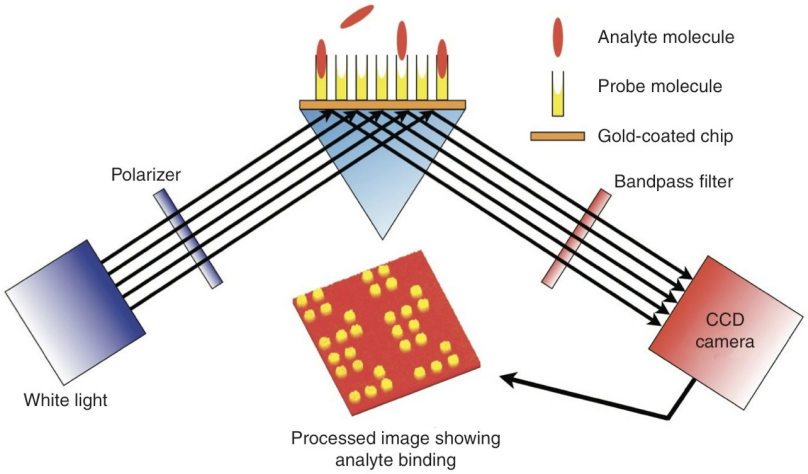
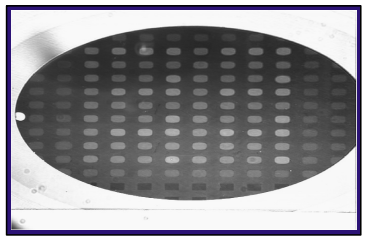
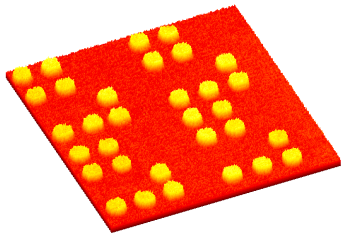
Multiplexed Surface Bioaffinity Measurements - SPRI Microarrays

Surface Plasmon Resonance Imaging (SPRI) of DNA microarrays

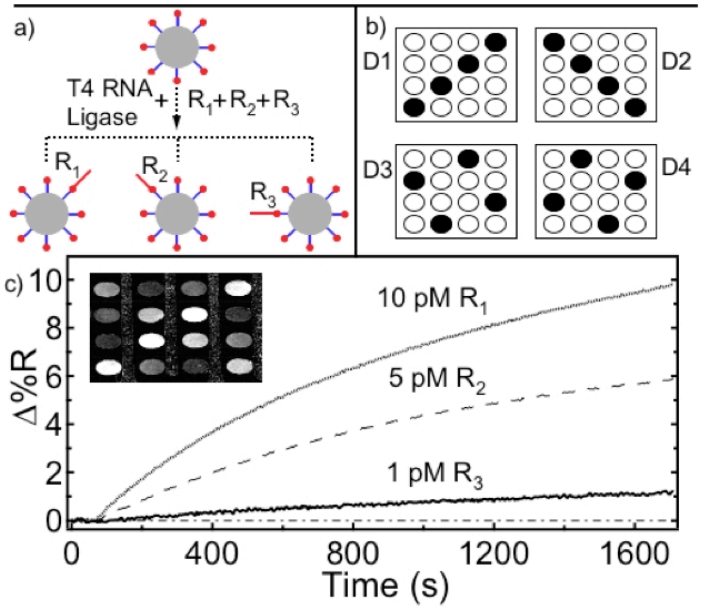




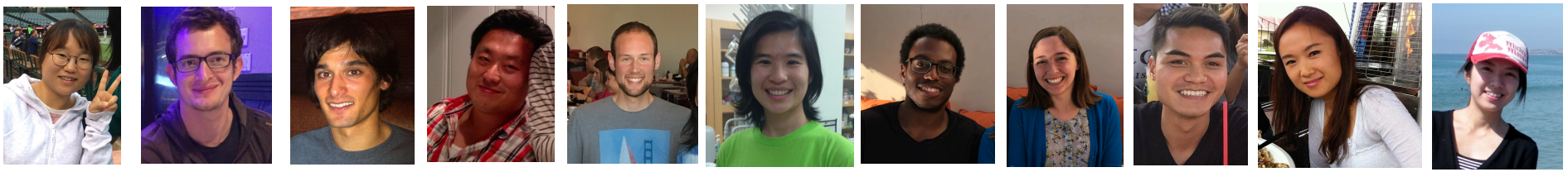


SNPs, Genomic DNA

Multiplexed Nanoparticle-Enhanced SPRI detection of microRNA



Robert M. Corn - UCI Department of Chemistry



The Key Ingredient: Great Group Members and Collaborators!!!

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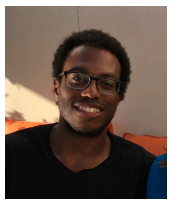

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