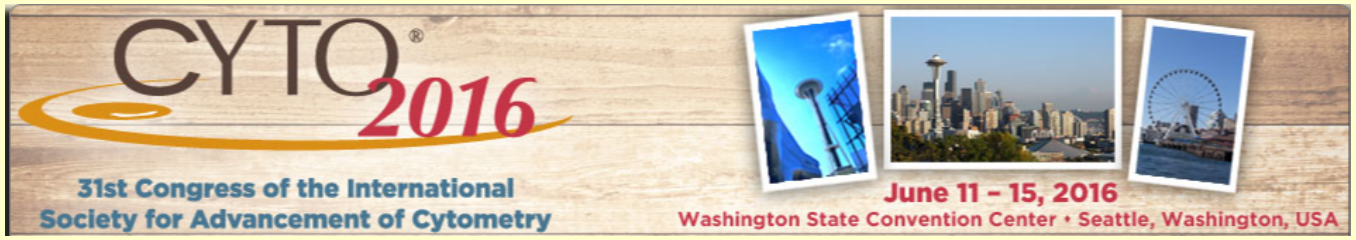


Optical Phase Detection for Nanoparticle Analysis

Workshop 11: Nanoparticle Characterization

June 13, 2016

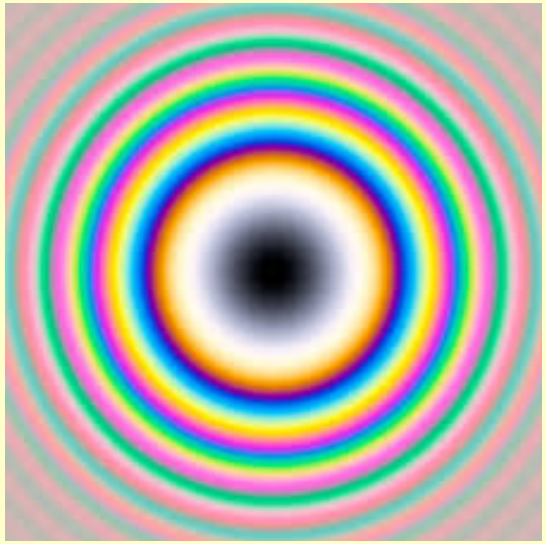
M. Yamamoto

Paul Robinson

PURDUE UNIVERSITY

MiFtek

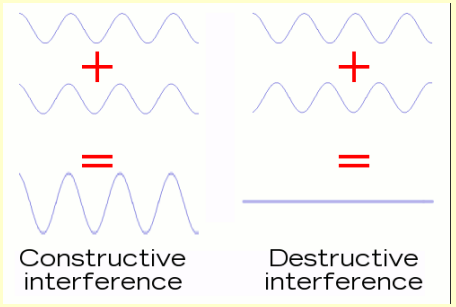
Blue sky and Newton Ring



Scatter intensity:

$$I = I_0 \left(\frac{1 + \cos^2 \theta}{2R^2} \right) \left(\frac{2\pi}{\lambda} \right)^4 \left(\frac{n^2 - 1}{n^2 + 2} \right)^2 \left(\frac{d}{2} \right)^6 ,$$

- **Essential principle of Flow Cytometry:**
- **relative value with calibration bead**

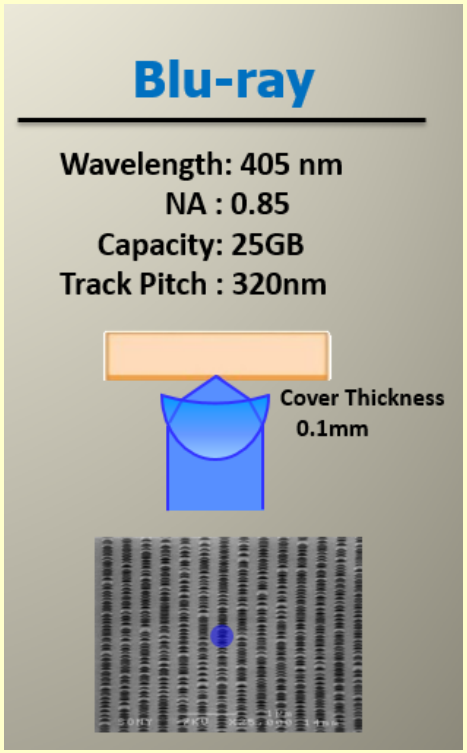


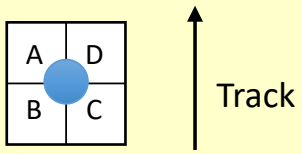
- **λ/2n : one way path (Transmissive)**
- **λ/4n : two way path (Reflective)**
- **defined by wavelength**
  λ/4 = 100nm at 405nm

PURDUE UNIVERSITY

MiFtek

Blu-ray Read-Out





HF = A+B+C+D
RPP =(A+B) – (C+D)
TPP =(A+D) – (B+C)

<Blu-ray Parameters>:

Reflective with 100um cover layer n=1.5

wavelength : 405nm NA= 0.85

Spot size : 250nm (FWHM)

Track pitch : 320nm control accuracy <±10nm

Pit depth : 60nm

Pit length : 150nm min.

Is it possible to detect Nano Particles ?

Blu-ray Standard Drive

Read Power = 0.30 mW

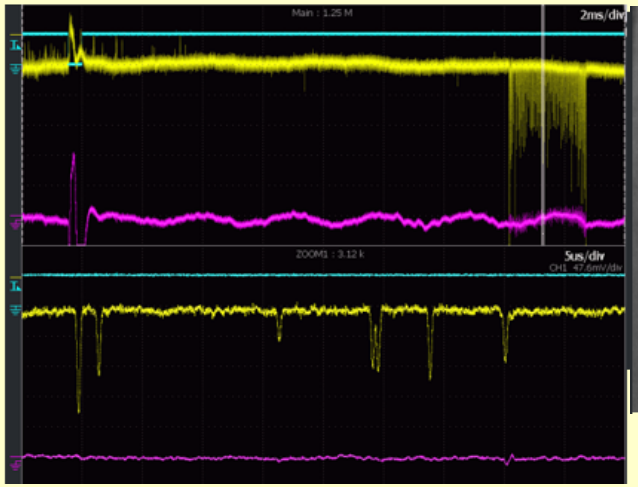
PURDUE UNIVERSITY

MiFtek

Gold particle Read signal on 500nm pitch Land & Groove

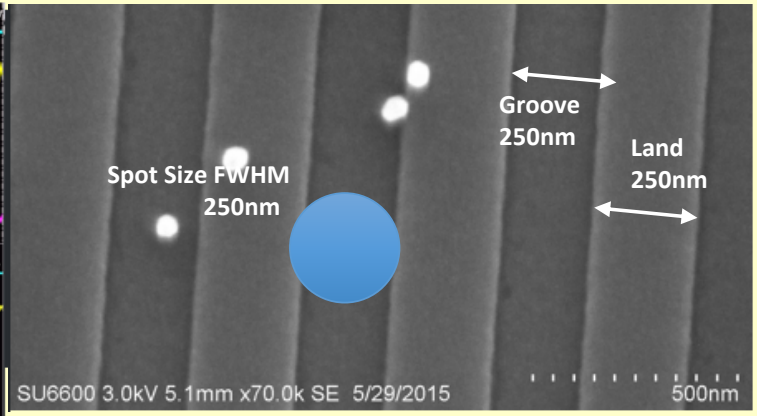
High spatial resolution is confirmed

Au 50nm HF & RPP

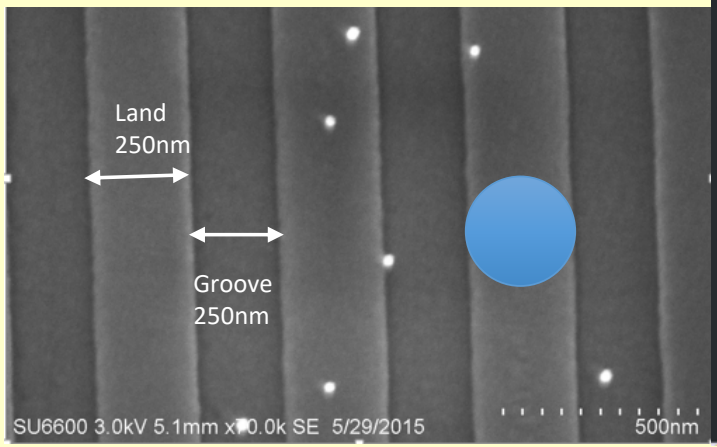


Au 50nm SEM picture

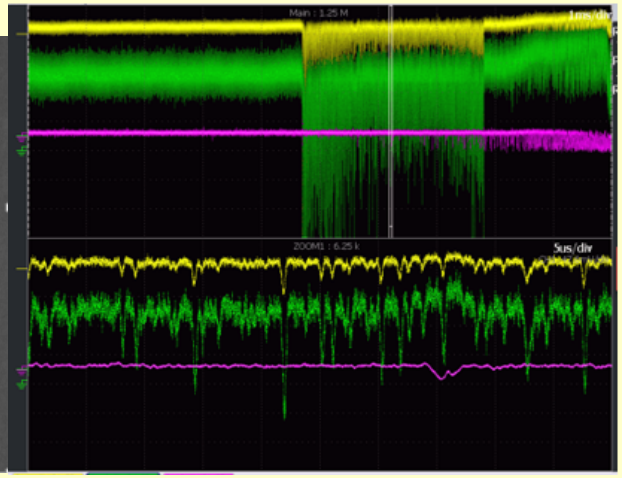
Depth=40nm



Au 30nm SEM picture



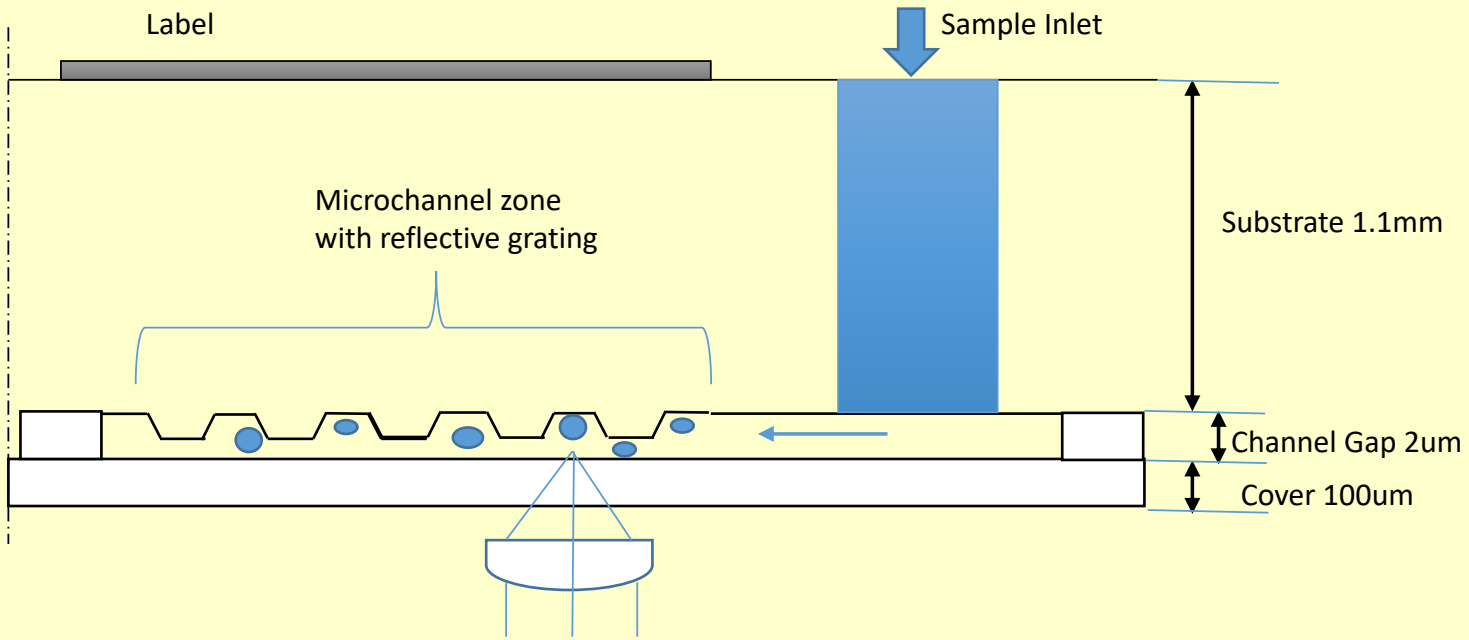
Au 30nm HF & RPP

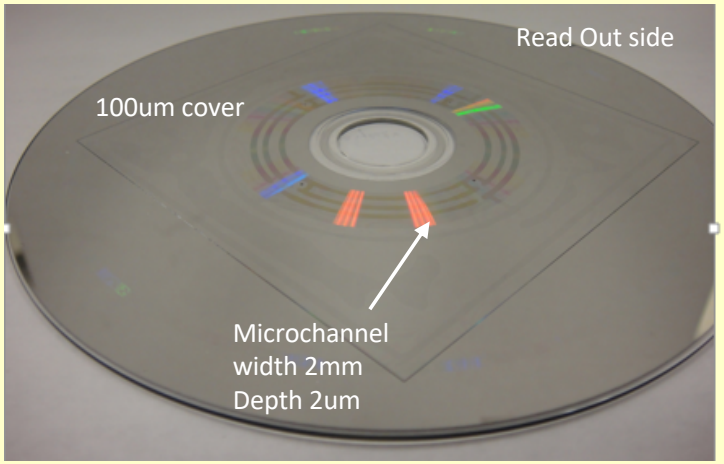


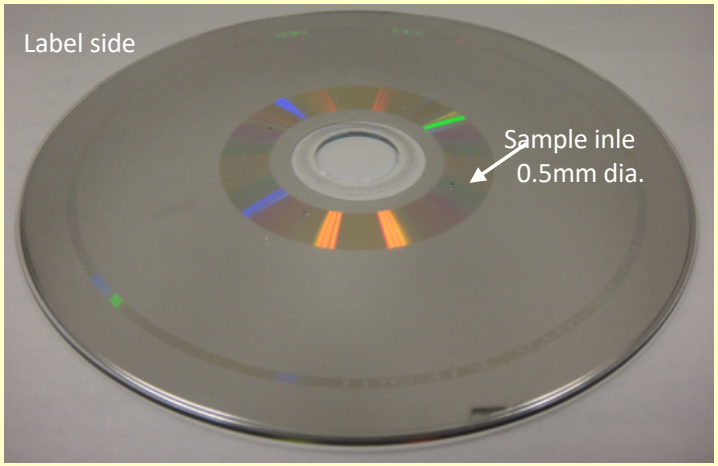
PURDUE UNIVERSITY

MiFtek

Micro channel with 2um height for liquid sample





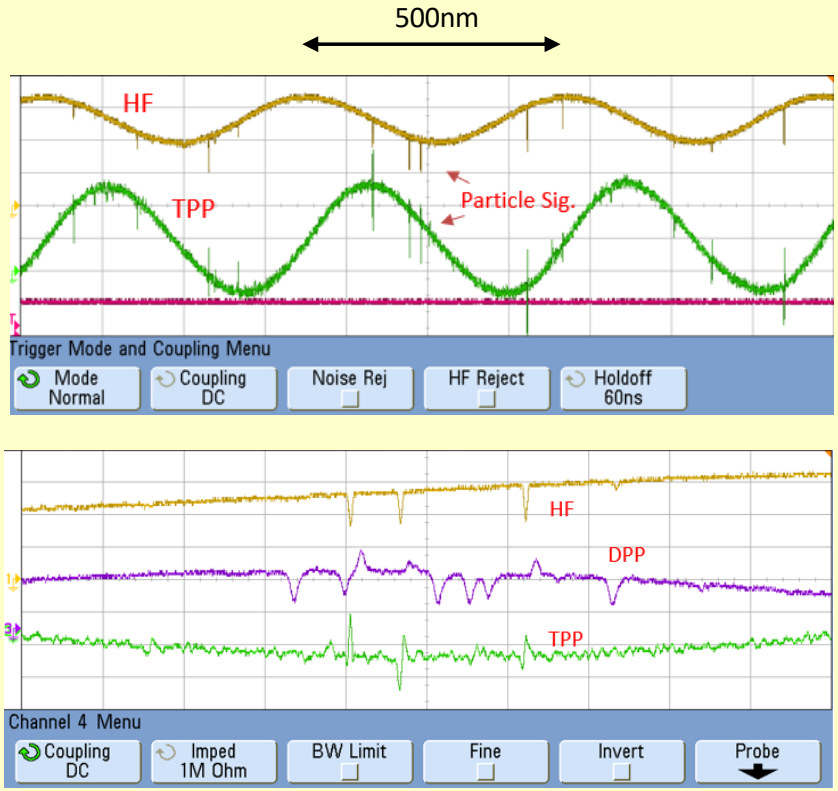


PURDUE UNIVERSITY

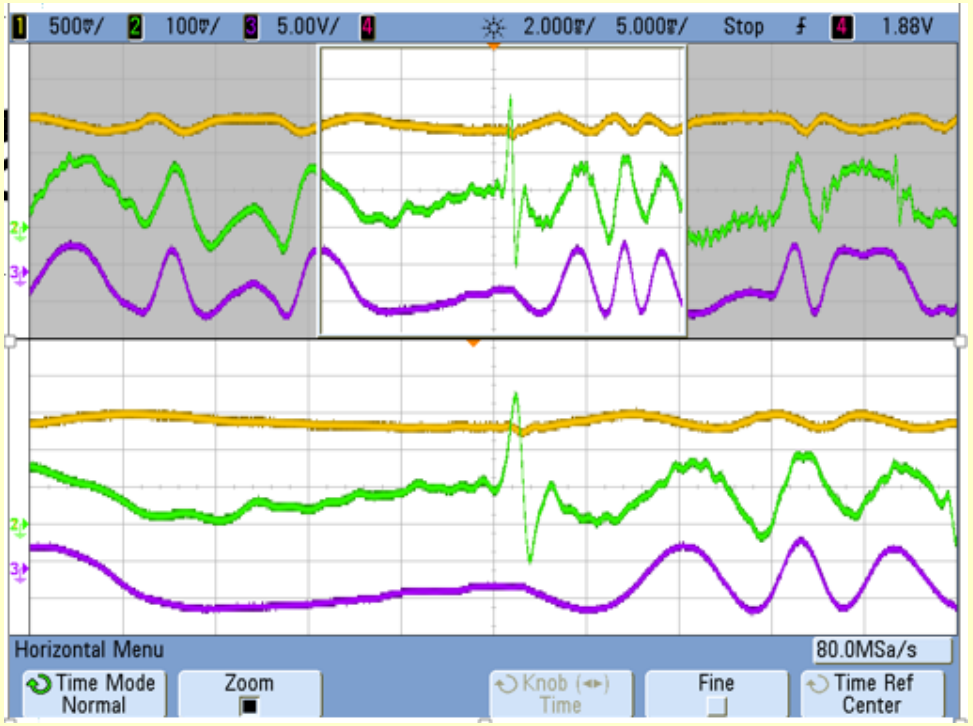
MiFtek

Particle Read out signal in Liquid(Water)

Gold 100nm signal in water



Polymer 100nm signal in water

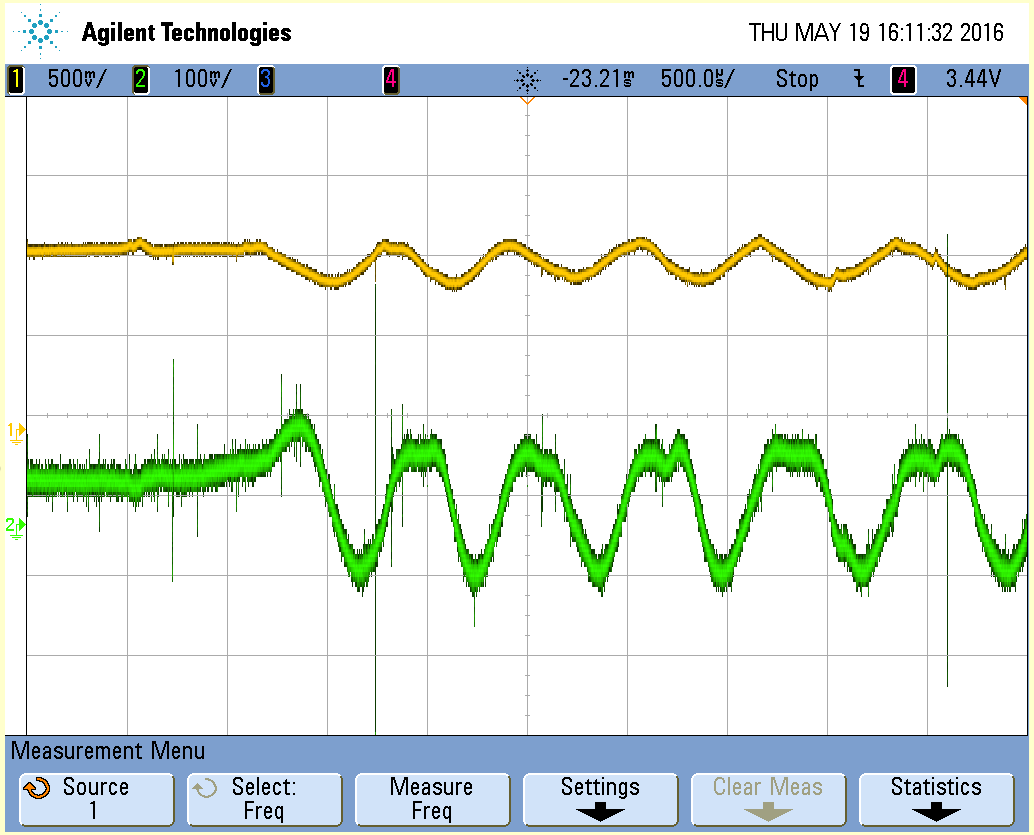


1. **Gold particle with large k modulates HF,RPP and TPP.**
2. **Transparent particle is detected by TPP signal.**
3. **Signal level is proportional to Δn x d.**

PURDUE UNIVERSITY

MiFtek

Firstly observed plasma sample signal: diluted x10 in water

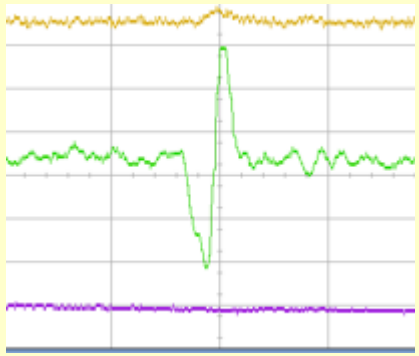


Channel radius=20.0 -22.0mm
Area size = 264 mm2
Channel Height= 2 um
Channel Volume= 0.5 ul

If concentration = 10^9 /ml

Estimated MV in channel= 0.5 million

Detected waveform



Reference: A Flow Cytometric Method for Characterization of Circulating Cell-Derived Microparticles in Plasma

PURDUE UNIVERSITY

MiFtek

Summary

1. Optical phase detection looks powerful for nanoparticle analysis.
2. Established mass production can provide low cost platform.
3. Many issues need to resolved for further steps;

   - Identification, Fl photon Detection, Analysis algorithm, Physical quality, etc.

Acknowledgement

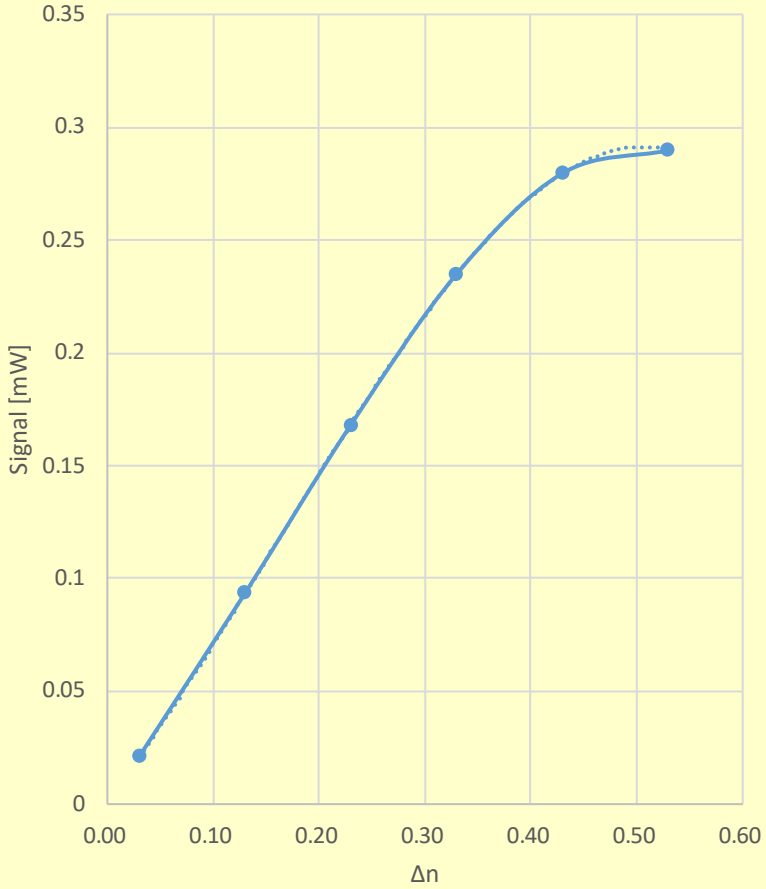
Sony DADC Terre Haute for custom disc design and manufacturing
Dr. A. Nakaoki for signal simulation
Purdue Flow Lab. members for sample preparation/signal analysis

PURDUE UNIVERSITY

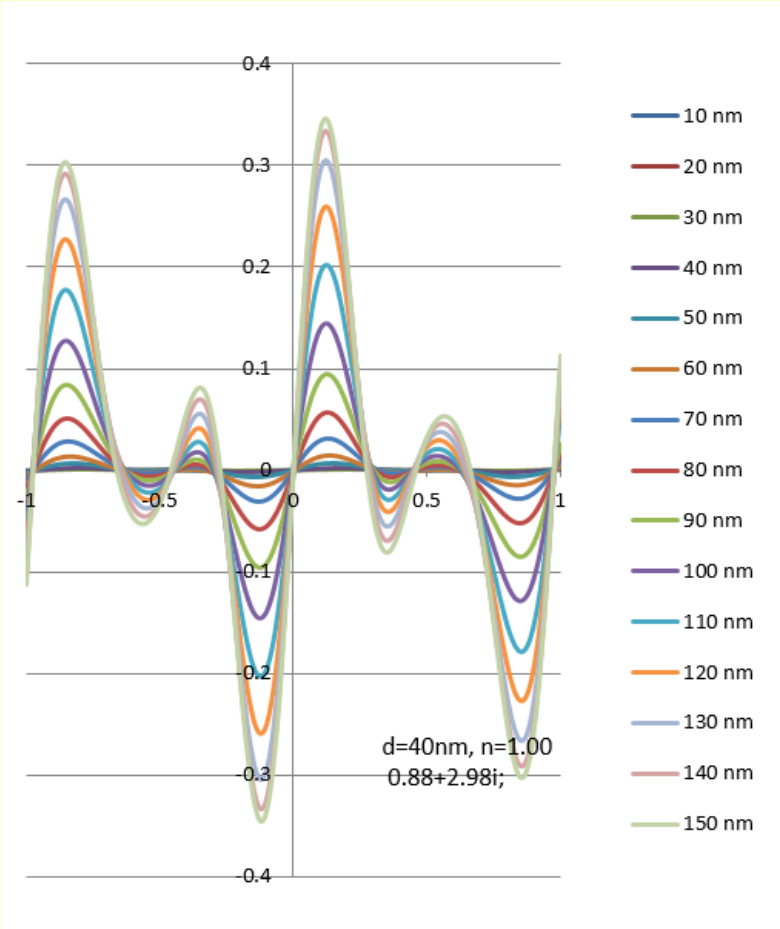
MiFtek

Simulated particle signal by Vector Theory

100nm particle TPP signal vs. Δn



Simulated TPP waveform vs. Particle size



PURDUE UNIVERSITY

MiFtek

The plasma samples were processed as follows:

1. whole blood (7 ml) collected in Heparin anticoagulant
2. serial centrifugation:
    a. 1800xg, 10 minutes
    b. transfer supernatant to a 15cc conical tube
    c. centrifuge 3000xg, 15 minutes
    d. transfer supernatant to a 15 cc conical tube
    e. centifuge 30000xg 5 minutes
3. aliquot plasma in 50ul aliquots
4. store at -80 degrees until analysis

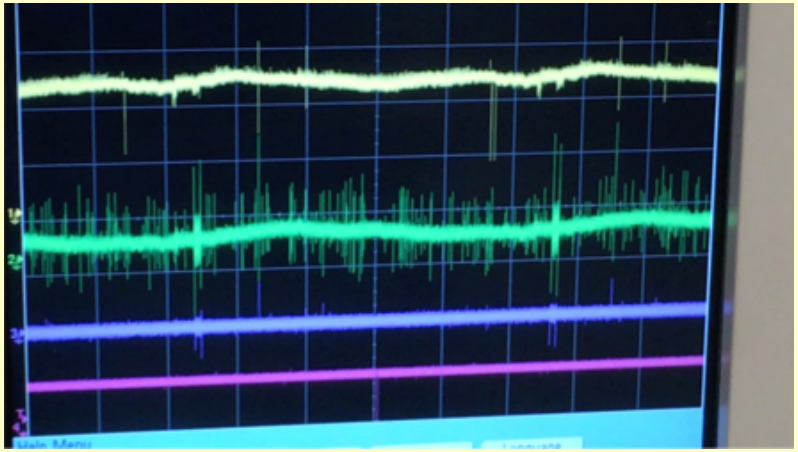
reference;

A Flow Cytometric Method for Characterization of Circulating Cell-Derived Microparticles in Plasma.

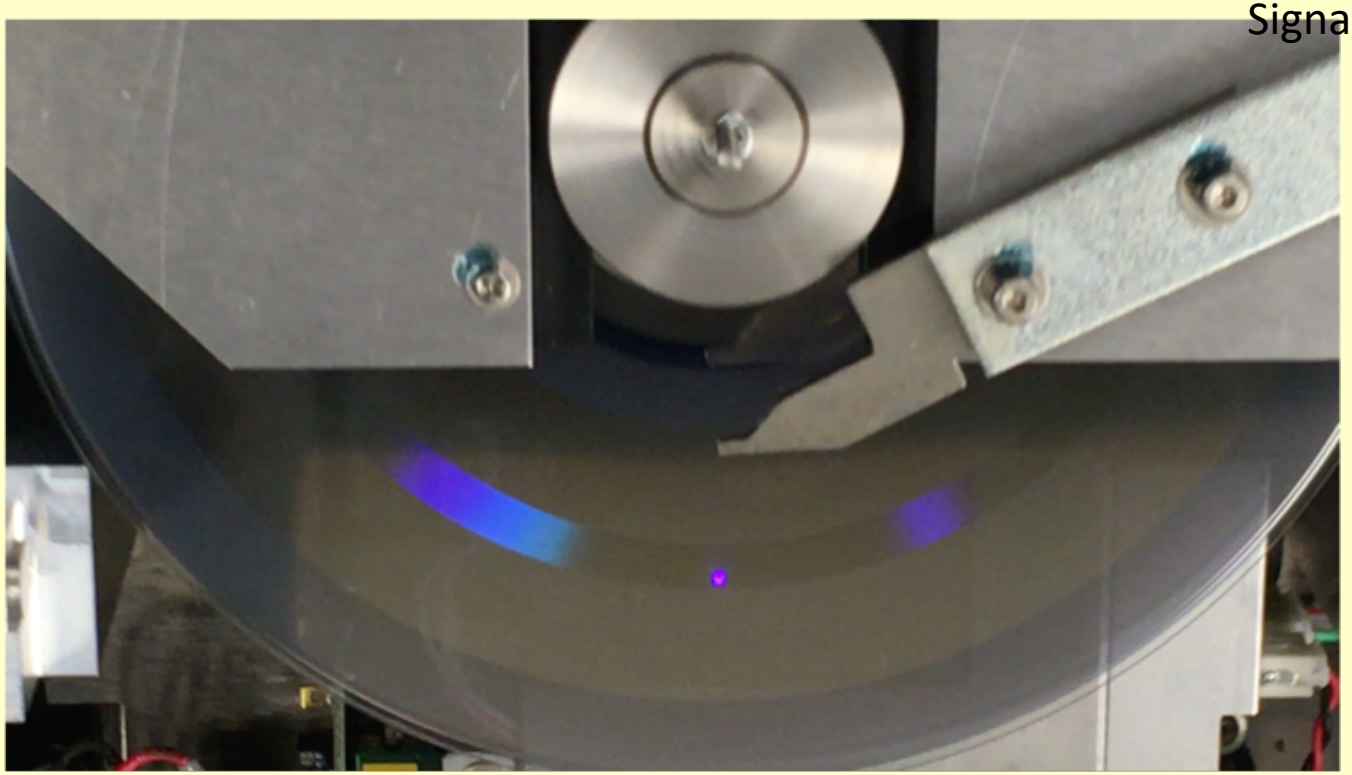
Morten Hjuler Nielson et al, Journal of Extracellular Vesicles 2014, 3:20795

Supplemental slides

Actual disc read



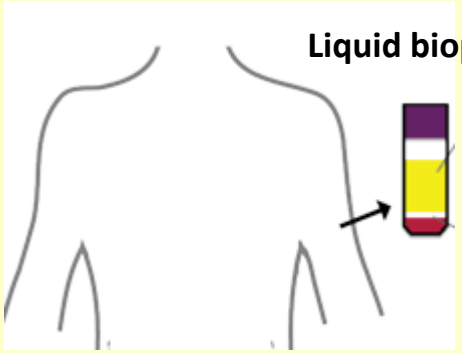
Signals on Oscilloscope



PURDUE UNIVERSITY

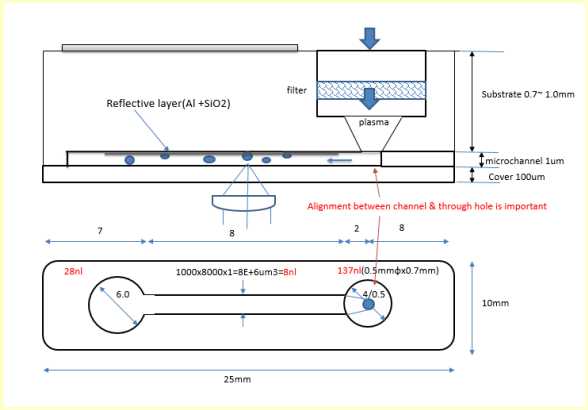
MiFtek

Liquid Biopsy Work Flow



Sample IN Whole blood → Cell Separation → staining → Microvesicles Measurement → Sorting → PCR → Targeted Sequencing

Slide glass shape LOC



X-Y scanning

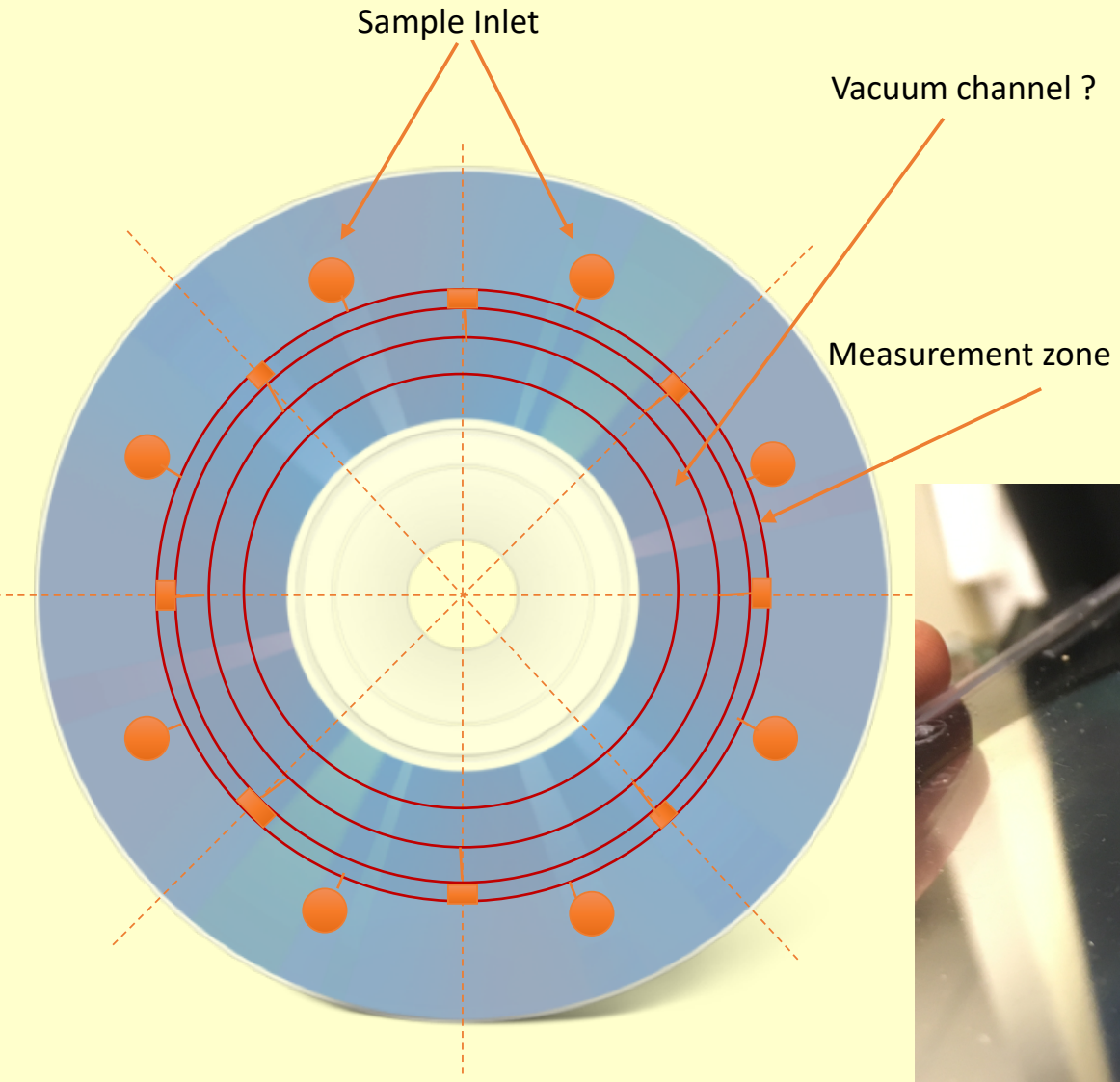
Disk shape LOC

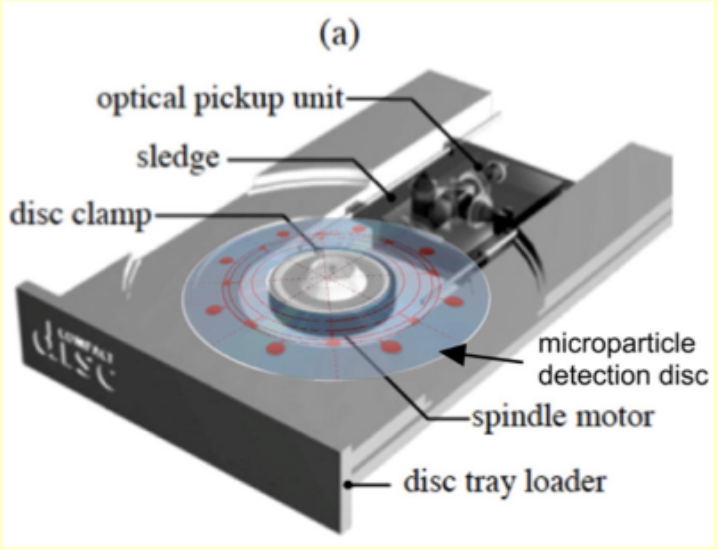
R-θ scanning

PURDUE UNIVERSITY

MiFtek

8 sample disk layout by modified DVD replication





PURDUE
UNIVERSITY