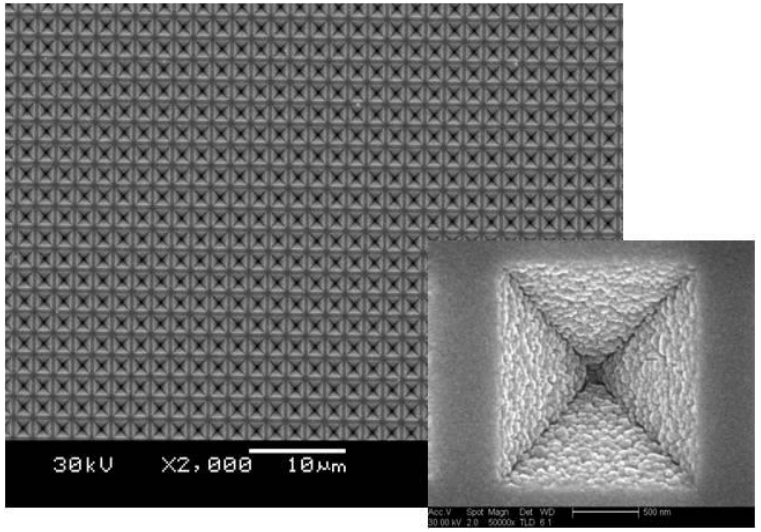
SERS: Instruments, Materials, and Applications for Defense and Security

Keith Carron
Metrohm Raman

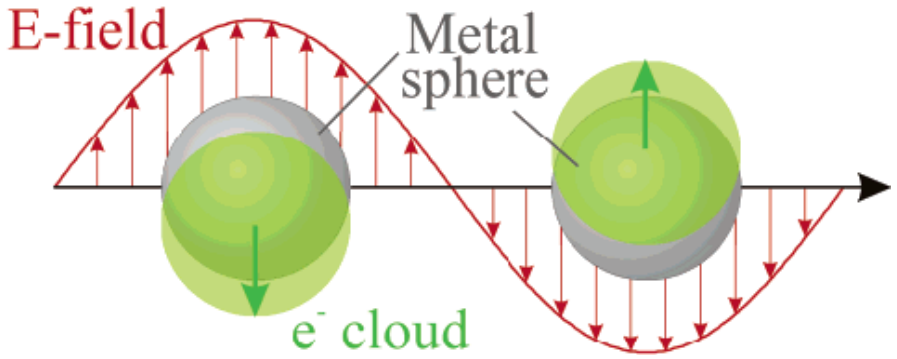


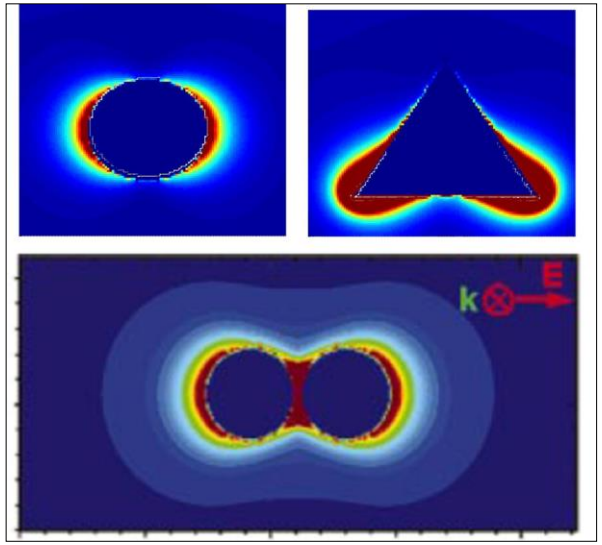
Topics

SERS: Instruments, Materials, and Applications for Defense and Security

SERS Introduction
Instrumentation
Substrates
- **Solutions**
- **Deposited**
- **Plasmonics**
- **Gaps**

Methods
- **ORS**
- **DRS**
- **Buoyant/Magnetic Separation**
- **Tags**





Haynes et al. Anal. Chem. (2005)

Instrumentation

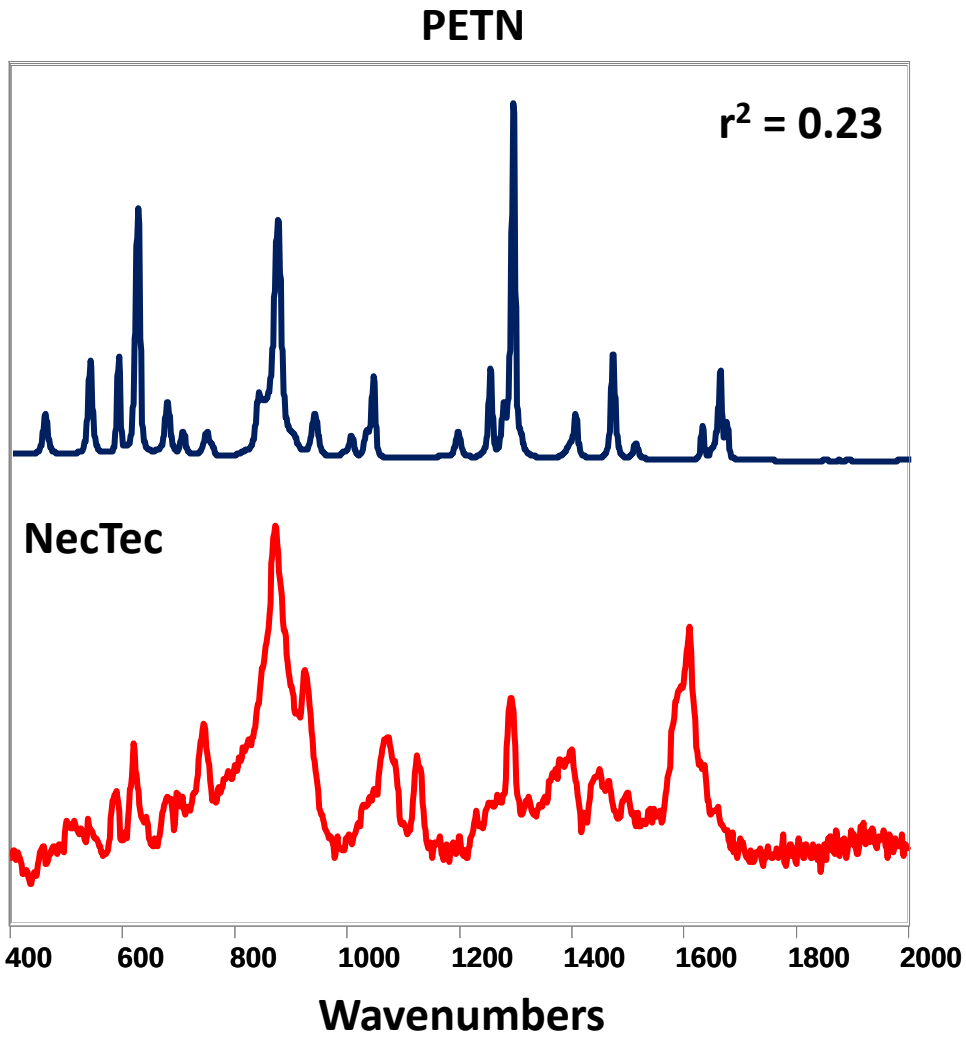
Laser Wavelength
- Gold – 638, 785
- Silver 532, 638, 785

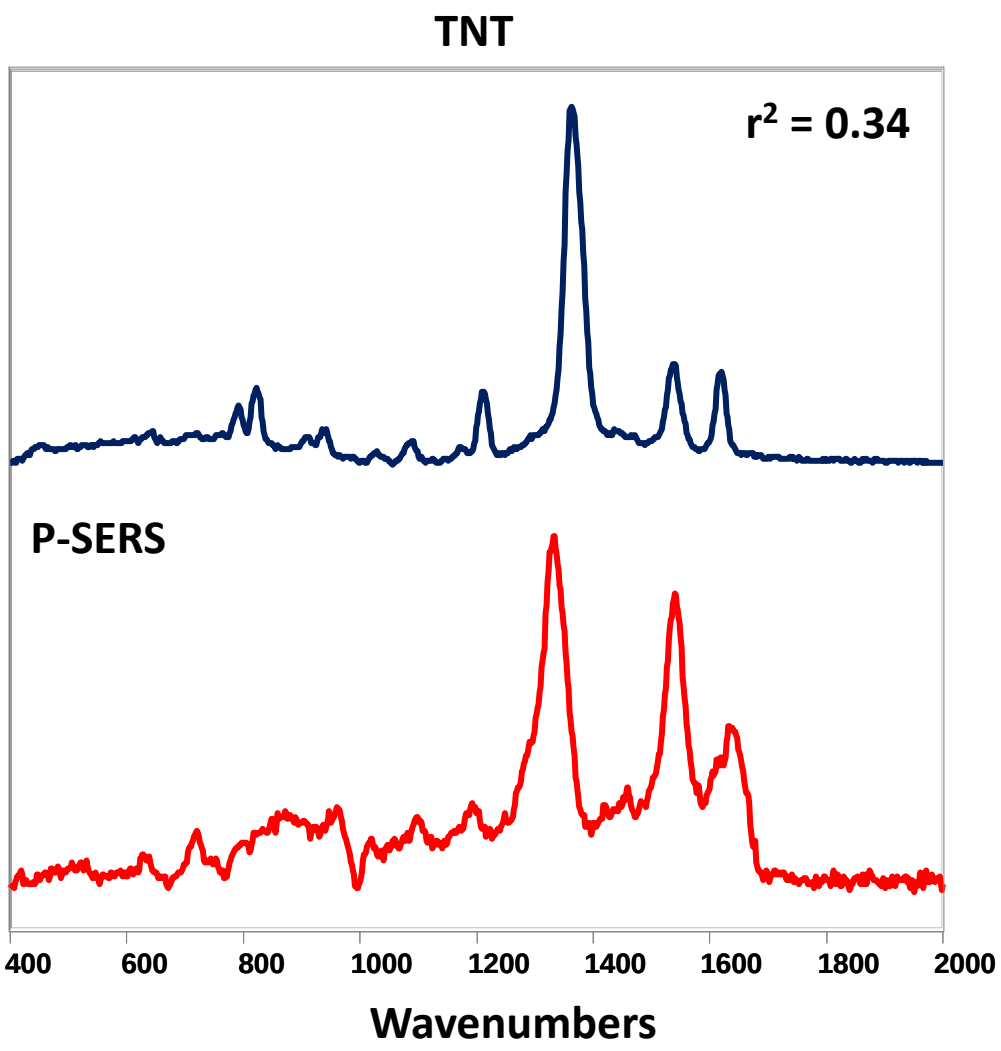
Laser Power
- SERS is sensitive to the laser power
- Ideal is < 10 mW
- Raster helps with the laser power and sensitivity

Spectral Resolution
- SERS broadens Raman bands
- Resolution between 10 and 20 wavenumbers is sufficient.

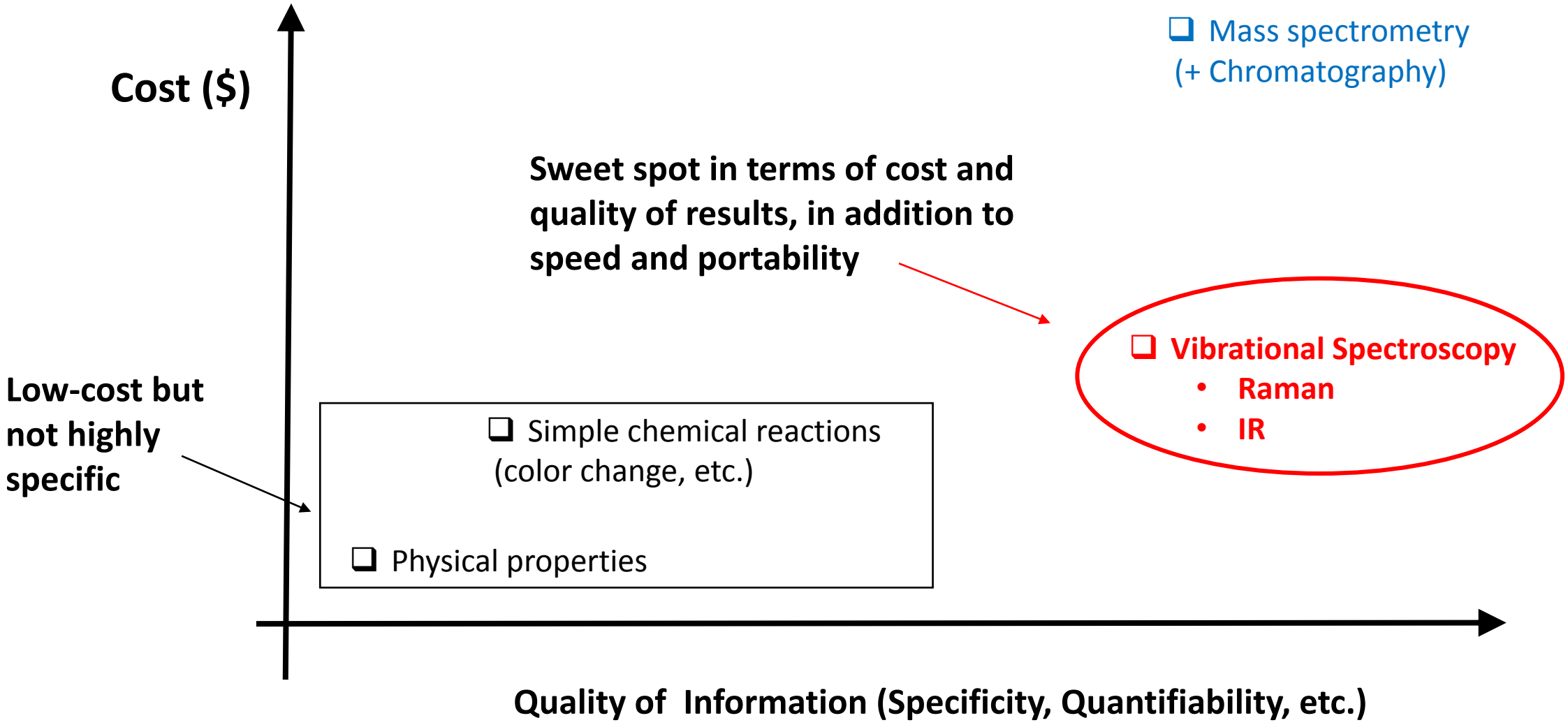
SERS spectra do not match normal Raman spectra
- New libraries are required

Instrumentation





Techniques to identifying unknown substances



Substrates

Colloidal Solutions

- Easy liquid dispensing
- Unstable over long periods (months)

Deposited Nanoparticles

- Easy to make and low cost
- Medium sensitivity

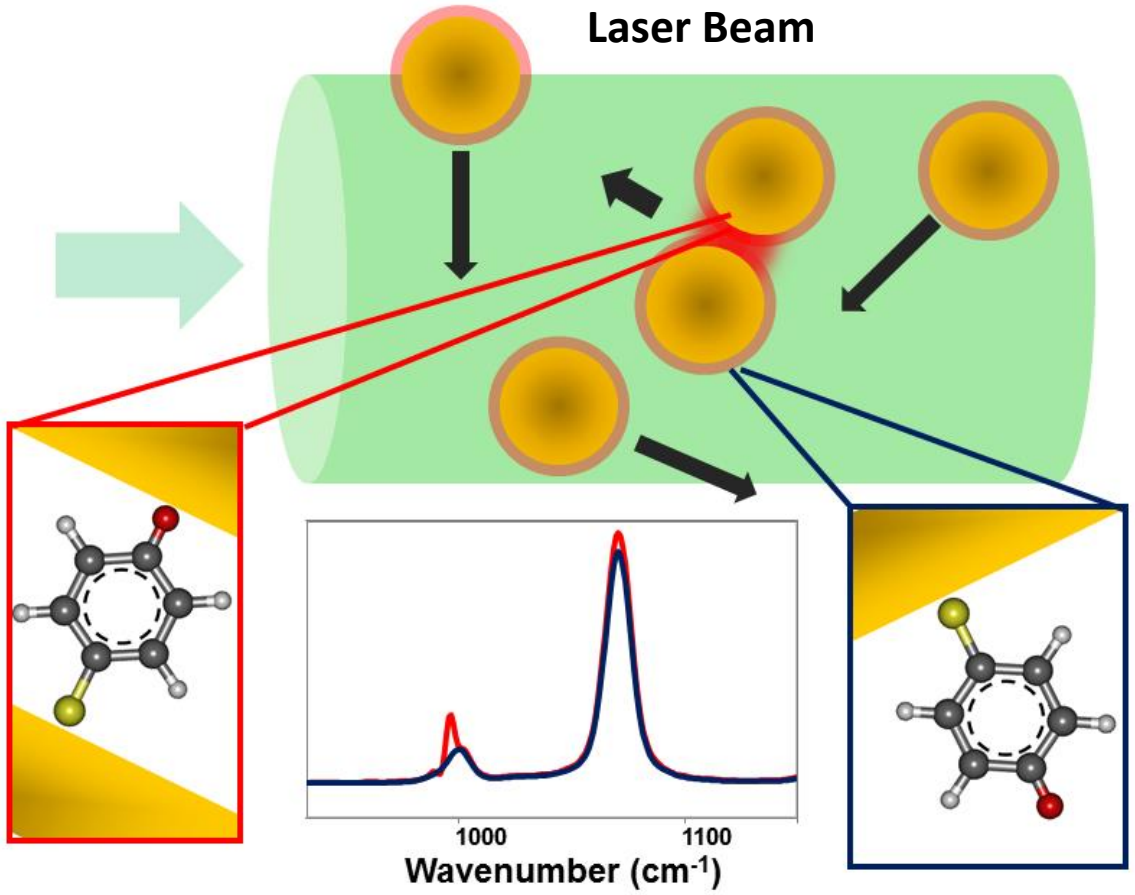
Plasmonics

- Difficult to make (high cost, but scalable)
- Low to medium sensitivity

Gaps

- Difficult to make (high cost, scalable)
- High sensitivity

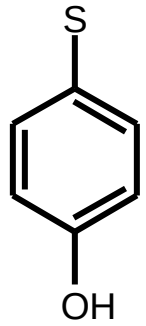
Substrates – Colloidal Solutions



Colloidal solutions are composed of primarily single nanoparticles with an anionic coating which creates a negative charge on the surface. The charge keeps the particles stable for a period of time.

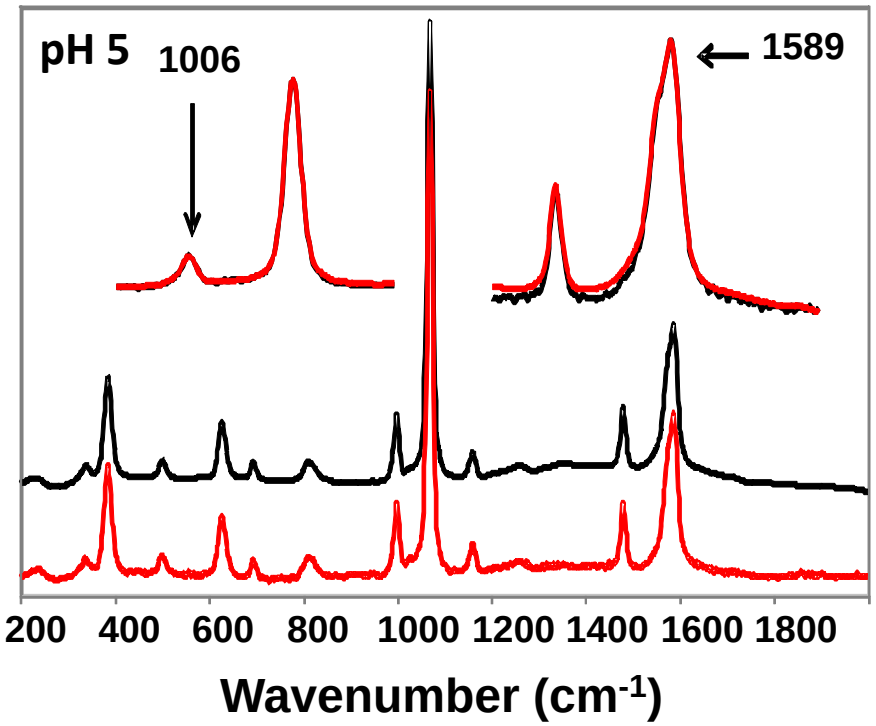
It is possible to observe aggregates and to show that aggregates produce 100x the signal of single particles. This is the concept behind “gap” substrates

Substrates – Colloidal Solutions

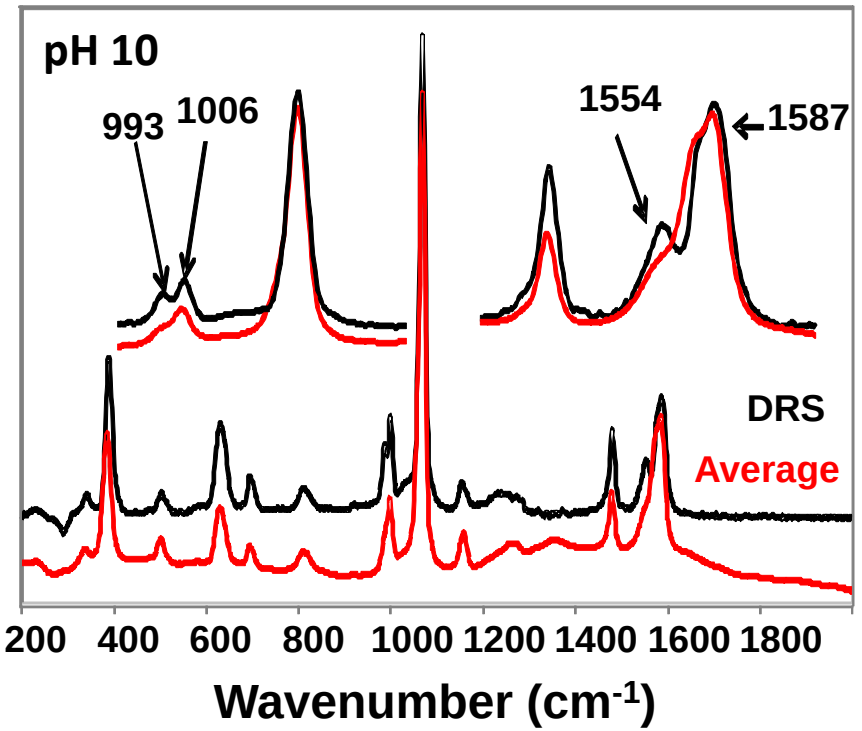


DRS (Dynamic Raman Scattering) is a way to capture rare events, like aggregation).

pH = 5



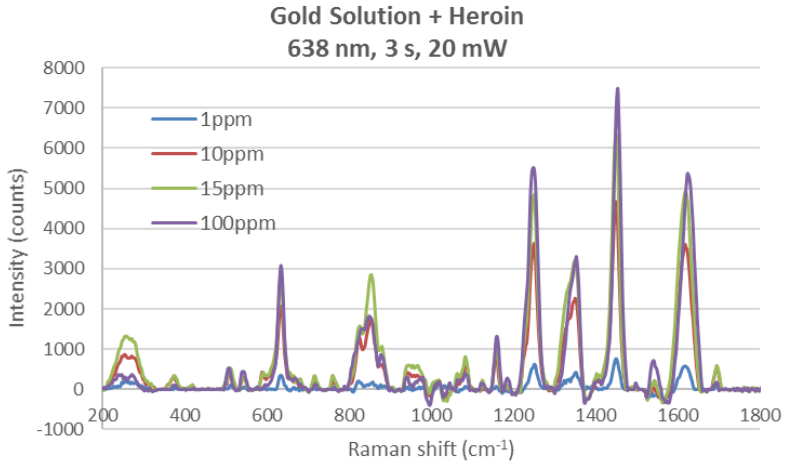
pH = 10

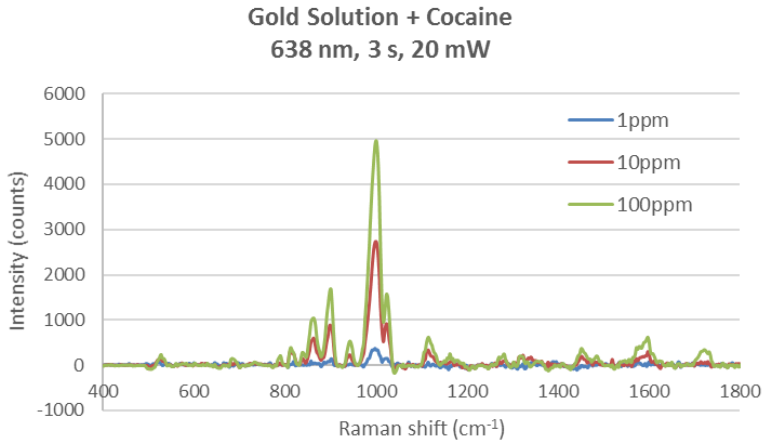


Substrates – Colloidal Solutions

- Liquid SERS
  - Aqueous Gold Nanoparticle Colloid
- Strong response to illicit drugs

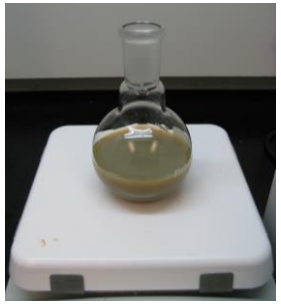
Ocean Optics SERS Offerings





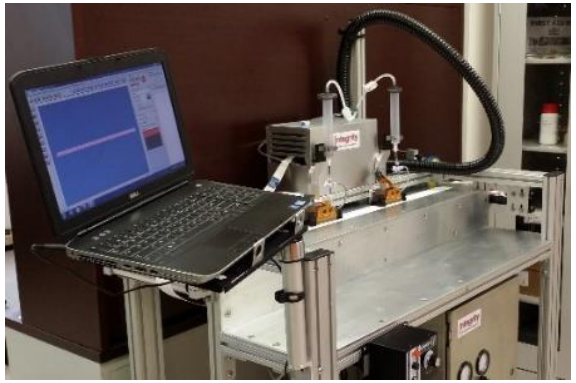
Anne-Marie.Dowgiallo@OceanOptics.com
Derek.Guenther@OceanOptics.com

Substrates – Deposited Nanoparticles



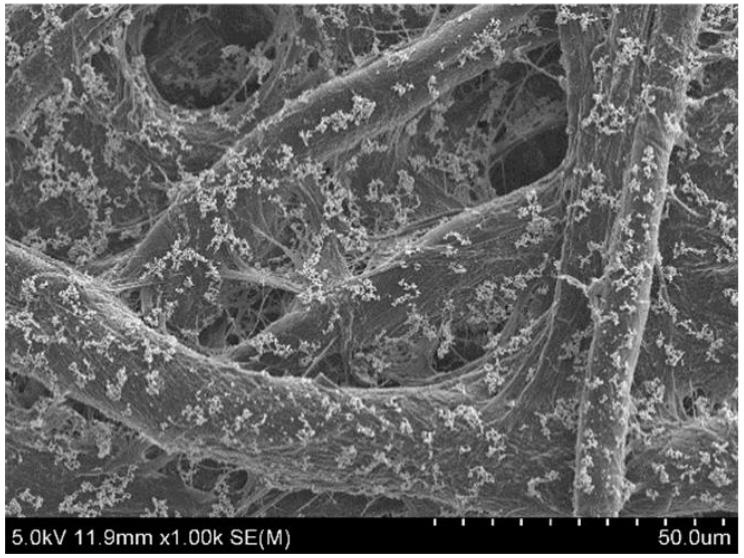
NP Ink

+



Printer

=



Hoppmann et al., *Methods*, 63(3):219–224, 2013

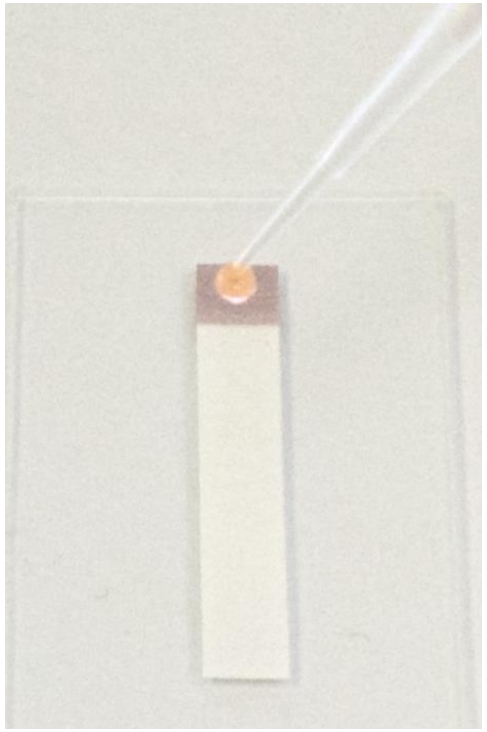
Diagnostic anSERS produces printable materials (P-SERS) with immobilized nanoparticles that produce medium sensitivity.

The advantage is that these materials have very low cost to produce. They can be produced for < $1.00.

Substrates – Deposited Nanoparticles

Metrohm Raman

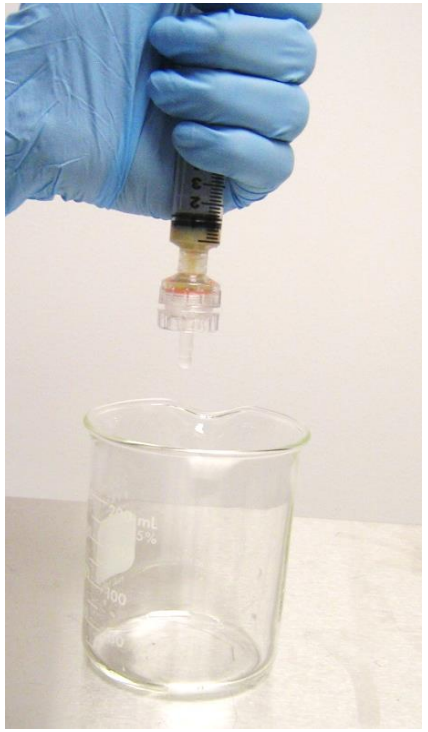
Pipetting



Swabs

Dipsticks

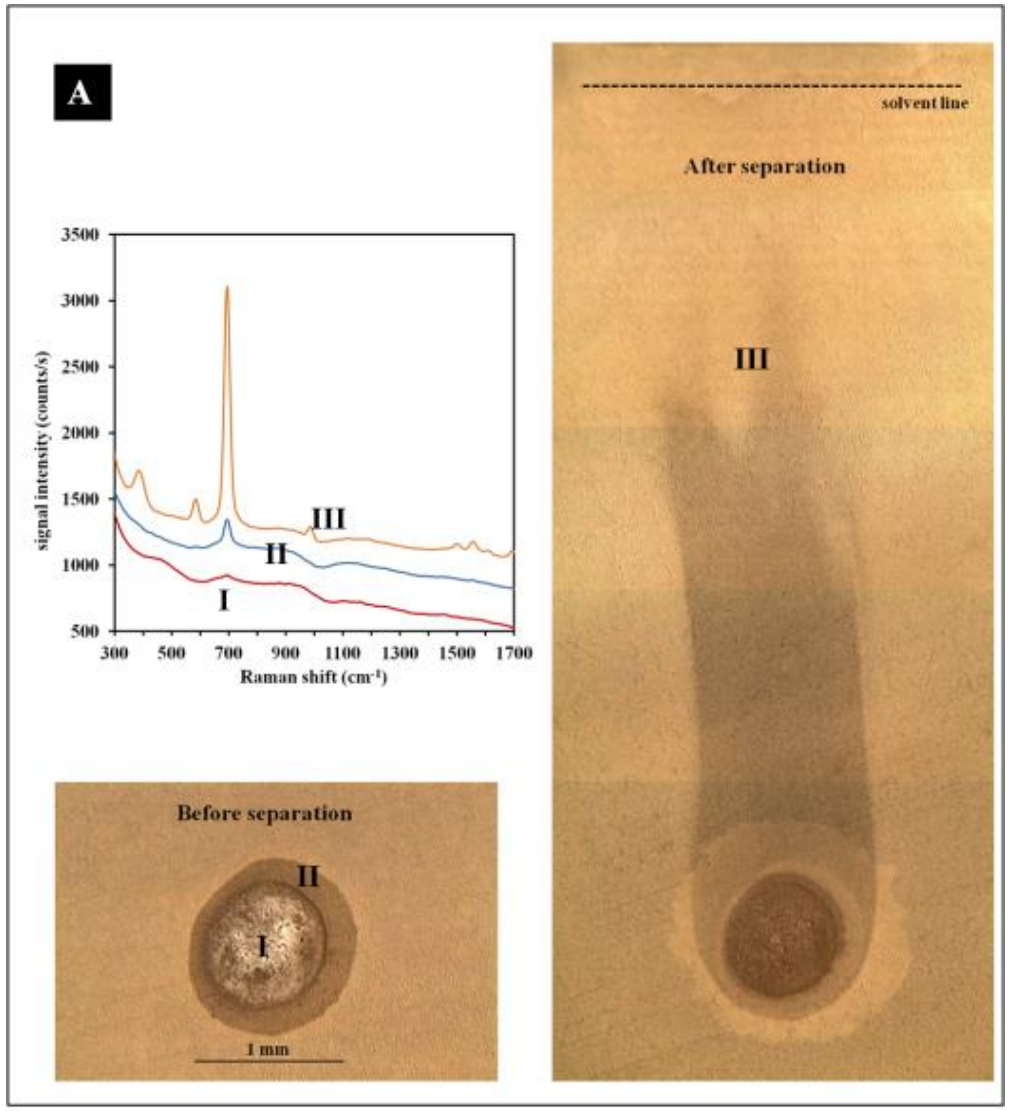
Filters



Substrates – Deposited Nanoparticles

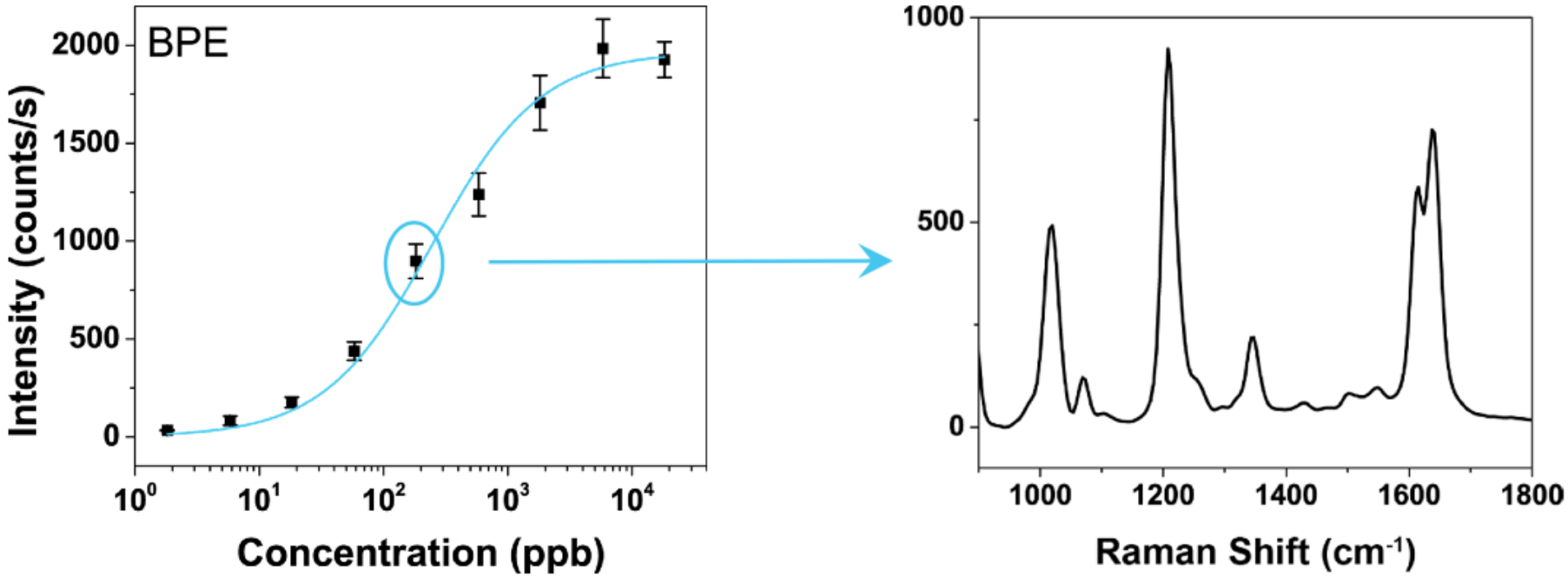
Separation of complex samples. Combination of chromatography and SERS.

e.g. Melamine in infant formula. Solvent is 0.1 N HCl.



Qualitative and Quantitative

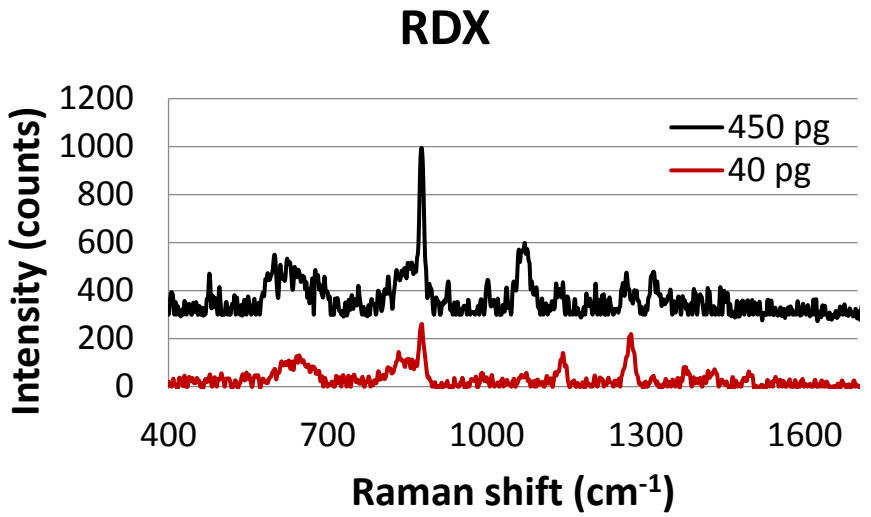
Langmuir Fit of spectral data

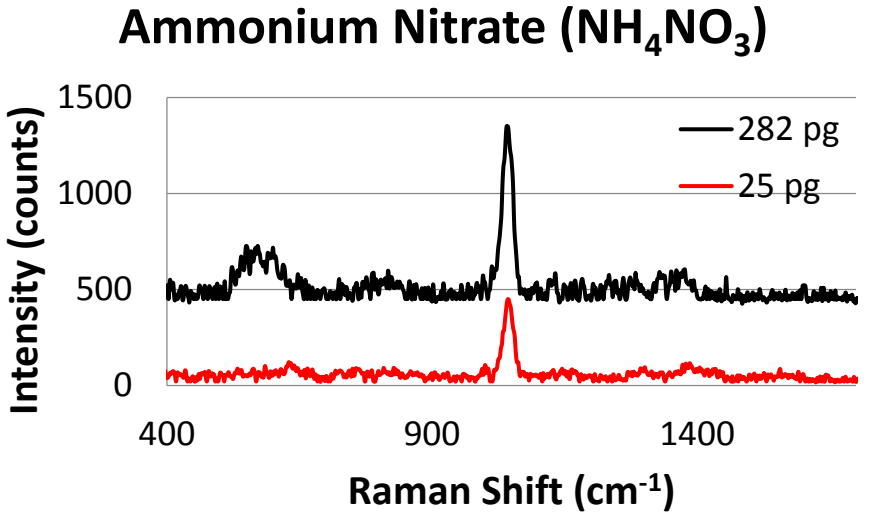


Substrates – Deposited Nanoparticles

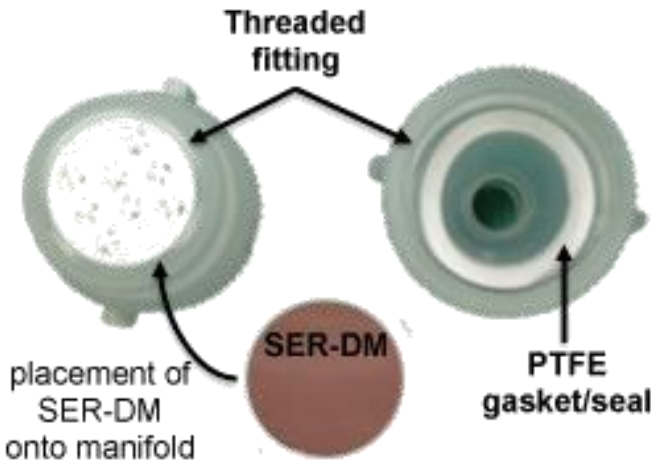
Ocean Optics Deposited Nanoparticles

- Available in 3 types:
  - Gold nanoparticles on quartz paper
  - Silver nanoparticles on quartz paper
  - Gold/silver alloy sputter-deposited onto structurally treated glass
- Repeatable response to explosives and explosive precursors

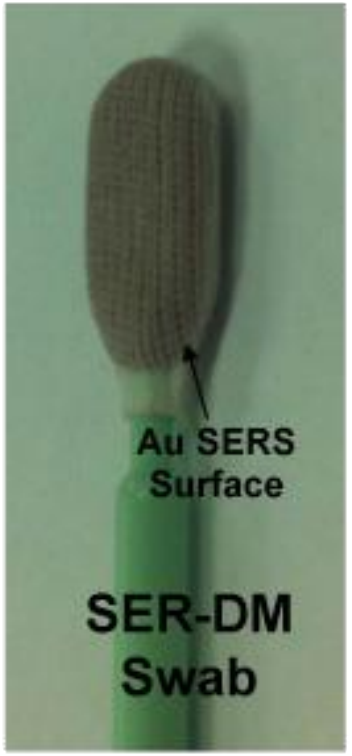


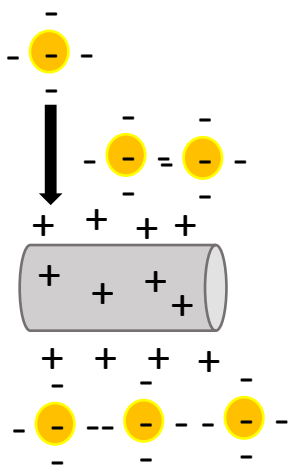


Substrates – Deposited Nanoparticles



Flexible Form Factors





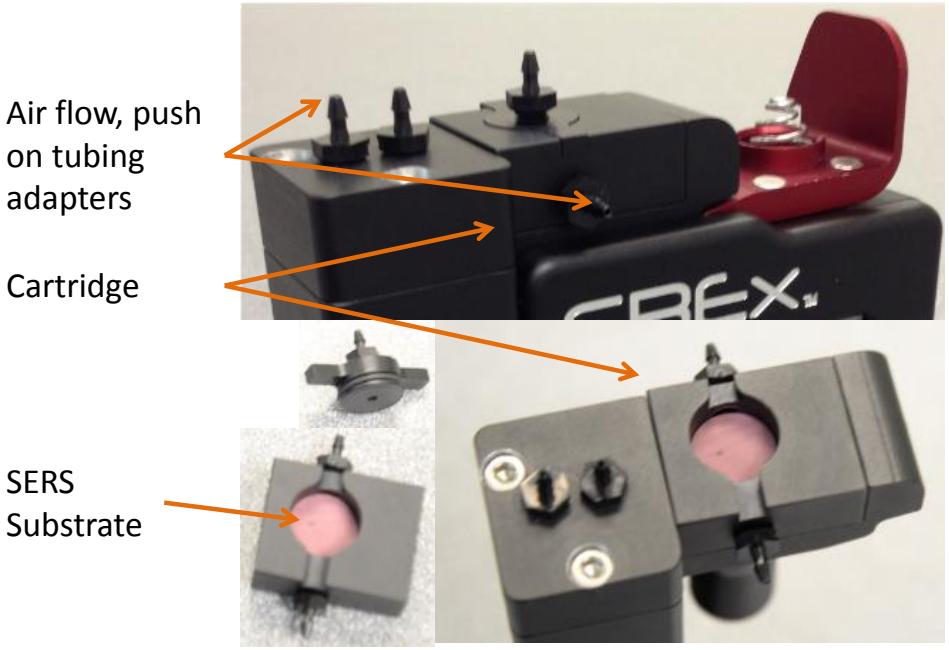
iFyber™

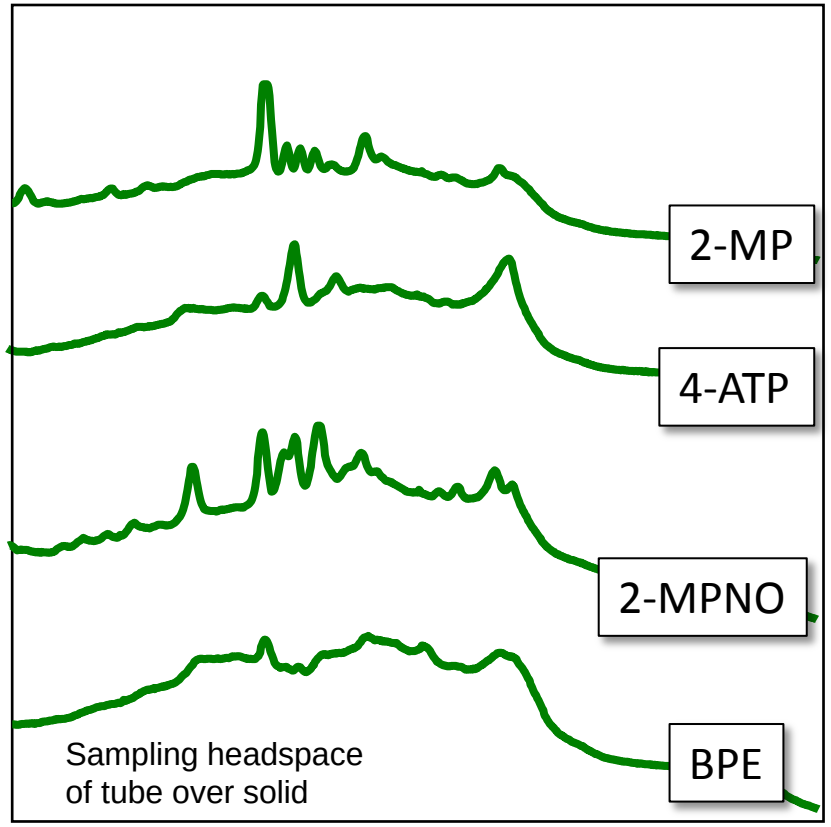
Substrates – Deposited Nanoparticles

VAPOR DETECTION

- iFyber SER-DM has been evaluated for vapor phase detection.
  - SBIR for the detection of chemical nerve agents using molecular sensor
  - Works with low vapor pressure solids

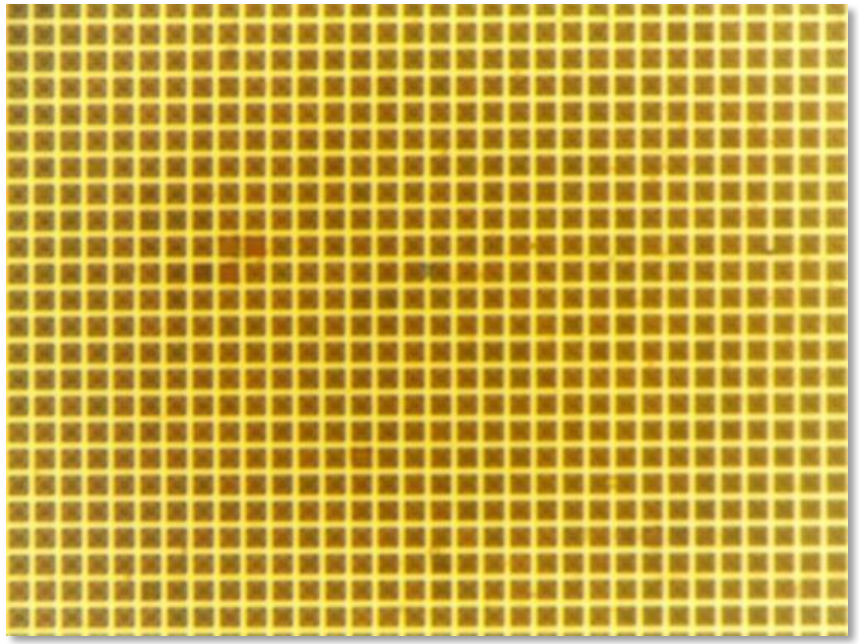
Sampling Device – 'Sniffer'

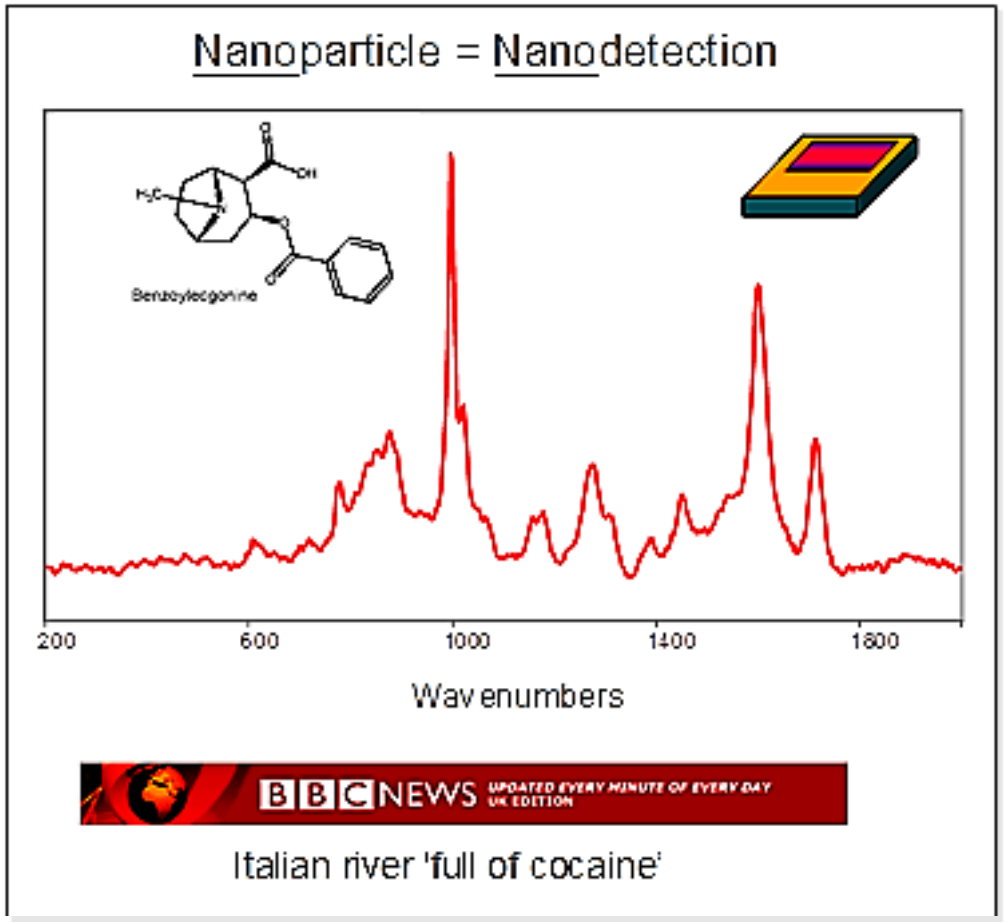




Substrates – Plasmonics

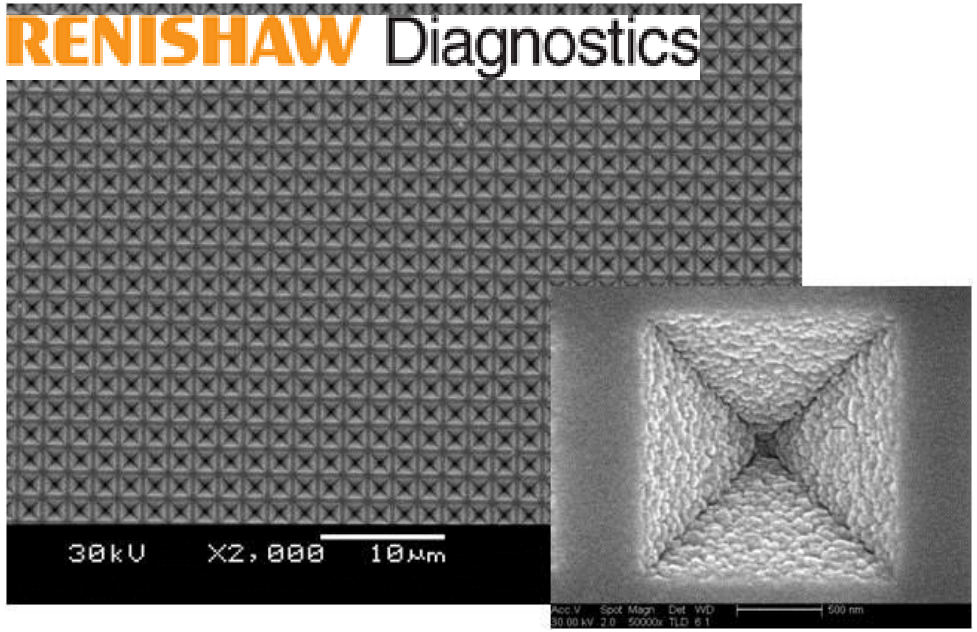
Clean metal surface. These do not have strongly bound anions from the reduction of Au^{3+} or Ag^{+}

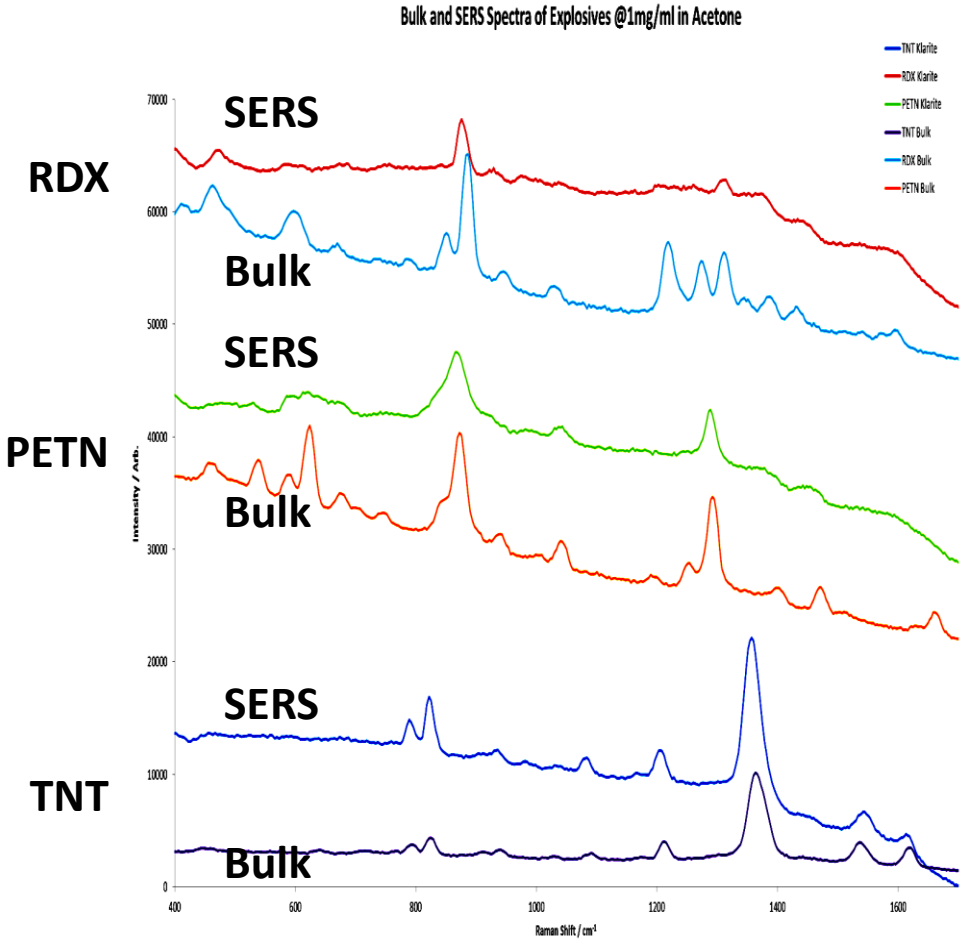




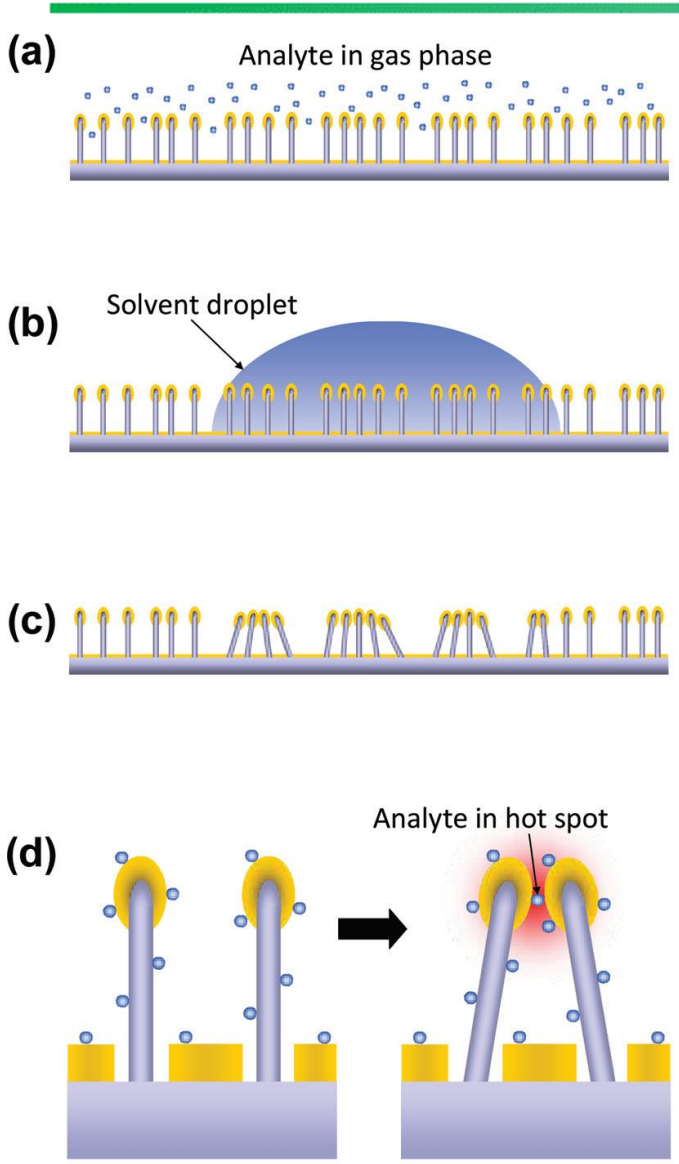
Substrates – Plasmonics

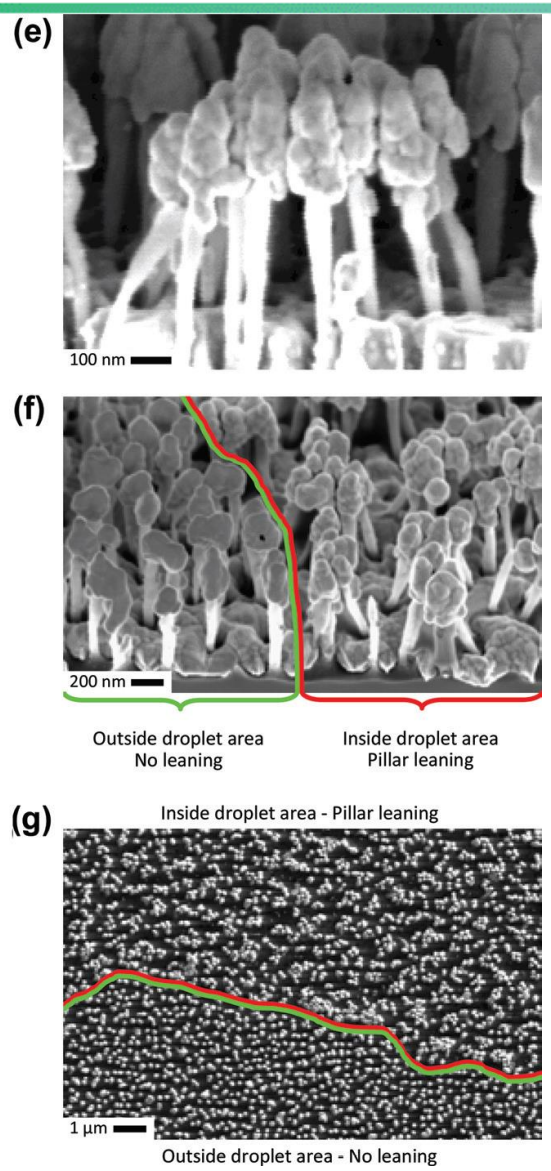
Plasmonic substrates produce SERS through periodic structures that collectively produce large local electric fields that enhance Raman scattering. The classic plasmonic substrate was Klarite produced by Renishaw Diagnsotics.





Substrates – Nanogaps



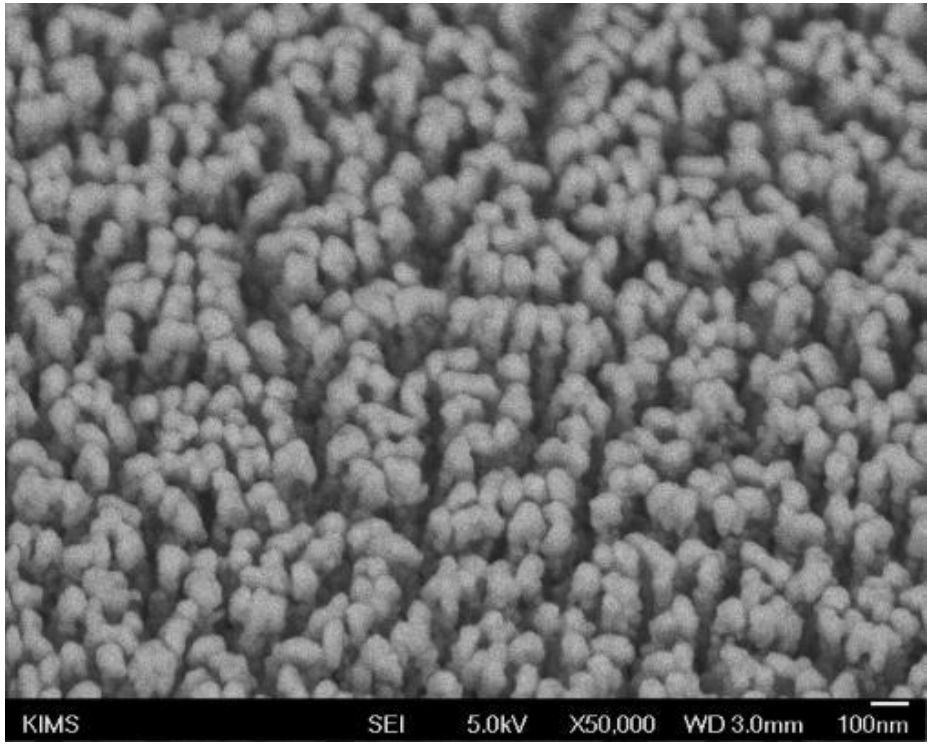


Large Area Fabrication of Leaning Silicon Nanopillars for Surface Enhanced Raman Spectroscopy

Michael Stenbæk Schmidt, Jörg Hübner, and Anja Boisen*

Adv. Mater. 2012, 24, OP11–OP18

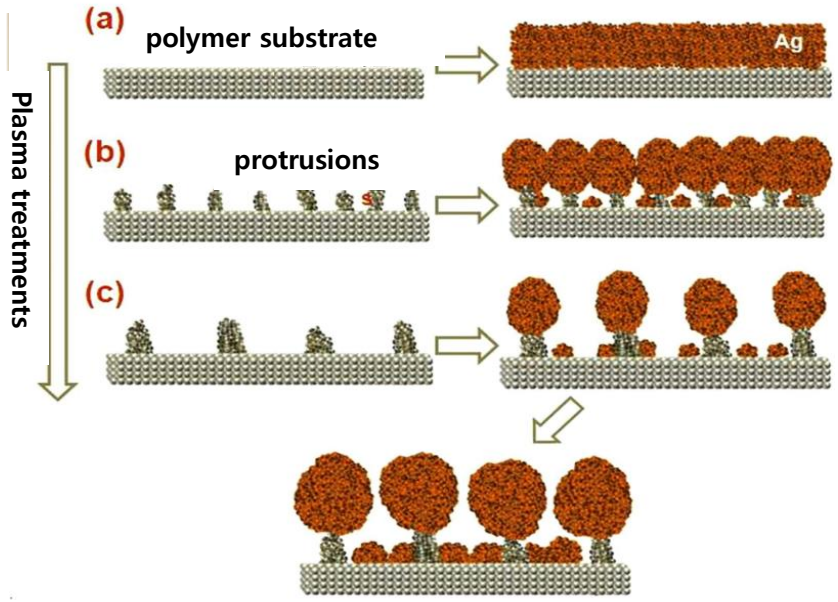
Korea Institute of Material Science



Substrates – Nanogaps

- Project : KIMS fund from Korea Gov.
- KIMStrate - high density nanogap SERS substrates on plastic films

✓ Maskless plasma etching of plastic films and plasmonic metal deposition
- Wafer-scale surface enhanced Raman scattering substrates
- High density nano-gap structures via grain growth on nm-scale protrusions

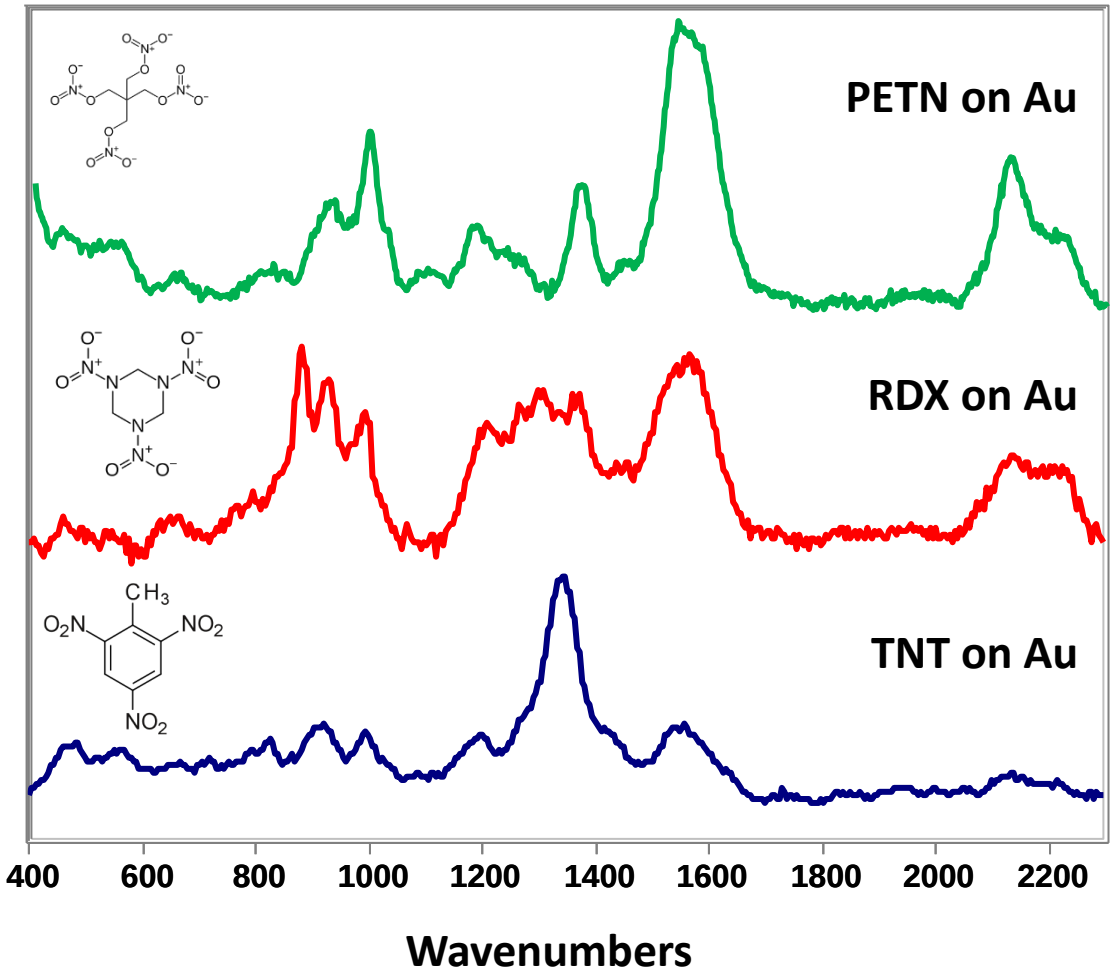


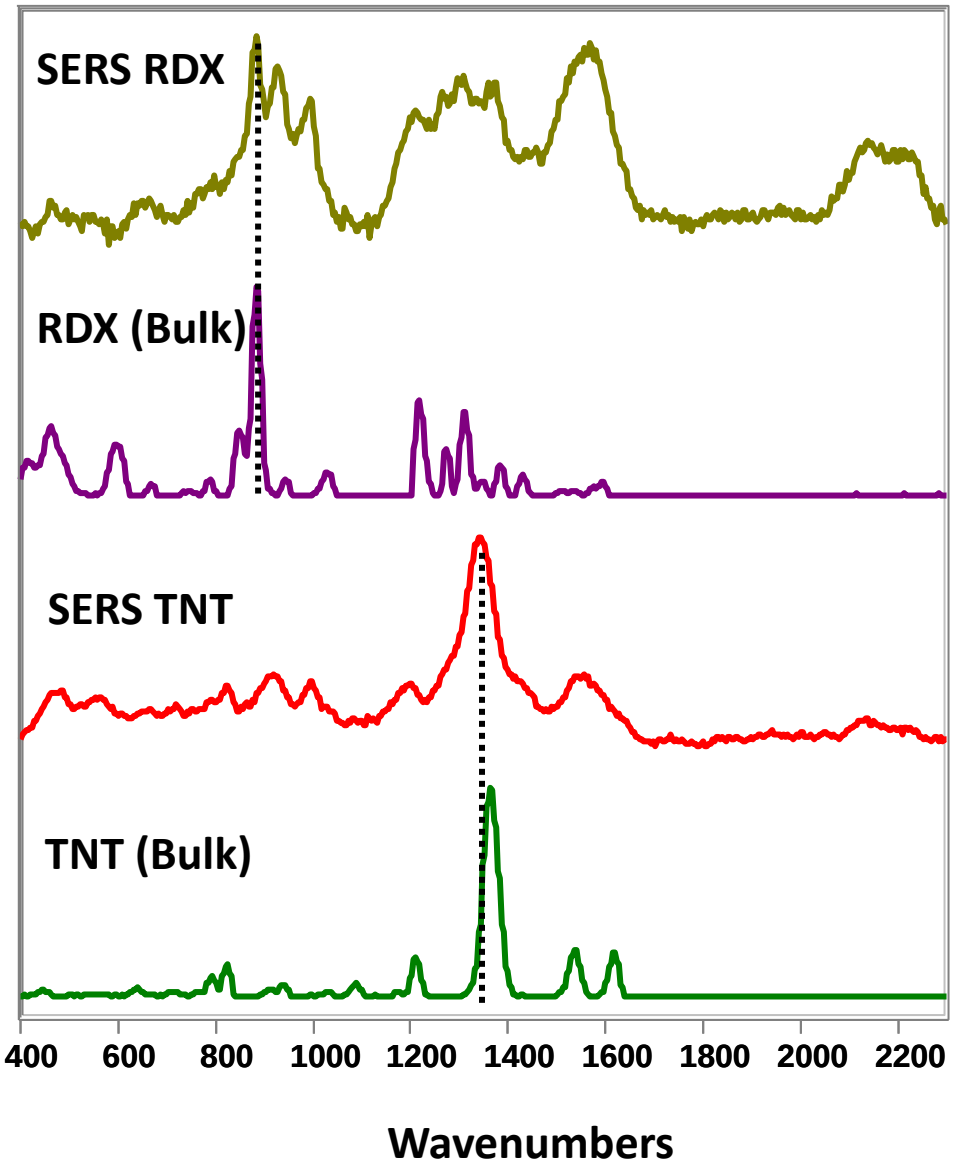
- **Ag SERS plates**
- Hot-spots density > 100/μm^2
- Nanogap less than 5 nm on average
- Enhancement factor ~3.3×10^7
- Standard deviations ~ 6.6%

Substrates – Nanogaps

Trace Explosives

SERS (1 mg/mL Acetone, 5 seconds)



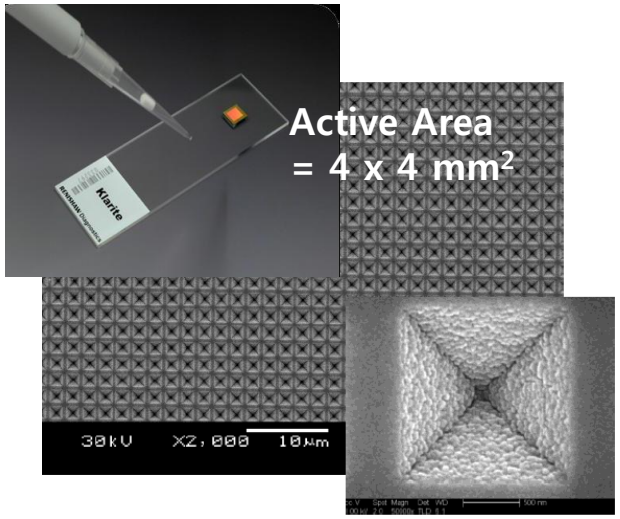


Substrates – Nanogaps

✓ Comparison with commercial products

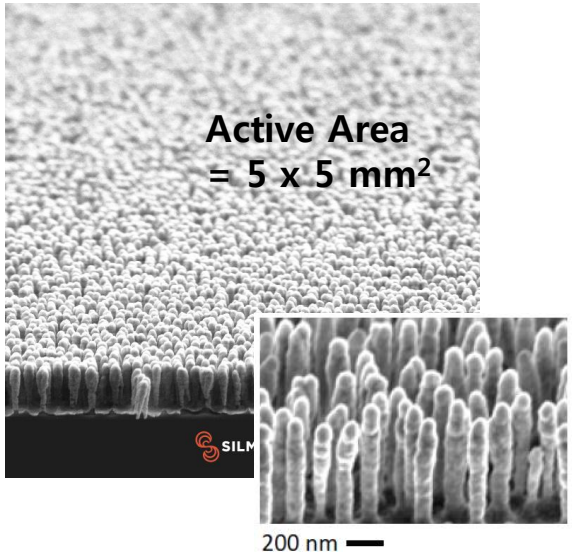
Klarite® Substrates (UK)

- micro-machined pyramid
- E.F. : ~10^5
- Uniformity(S.D.) : NA
- Price : 100$ /ea
- 1st gen. product



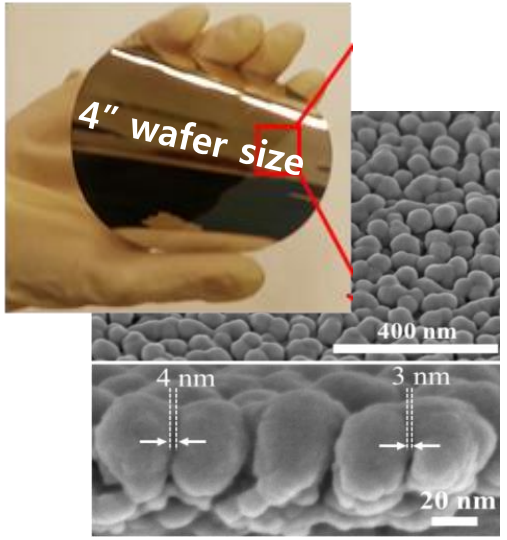
SERStrate® (Silmeco, Denmark)

- Dry Etching of Si
- E.F. : 7.8 x 10^6
- S.D. : 8%
- Price : $50/ea
- Nano pillar density ~ 20 μm^{-2}



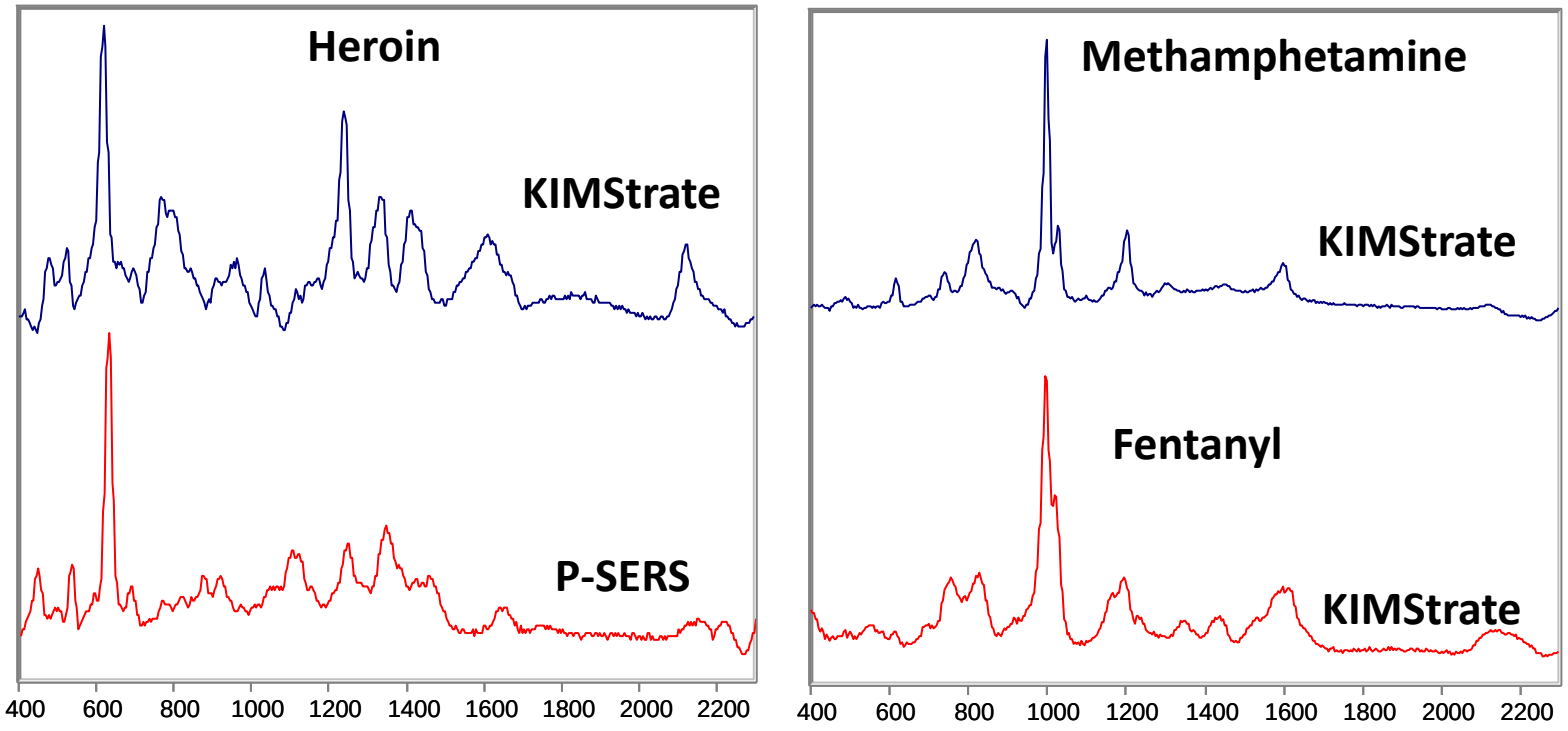
KIMStrate® (KIMS SERS)

- Nano island growth
- E.F. : 3.3 x 10^7
- S.D. : 6.6%
- Price < $5/ea
- NP density ~100 μm^{-2}



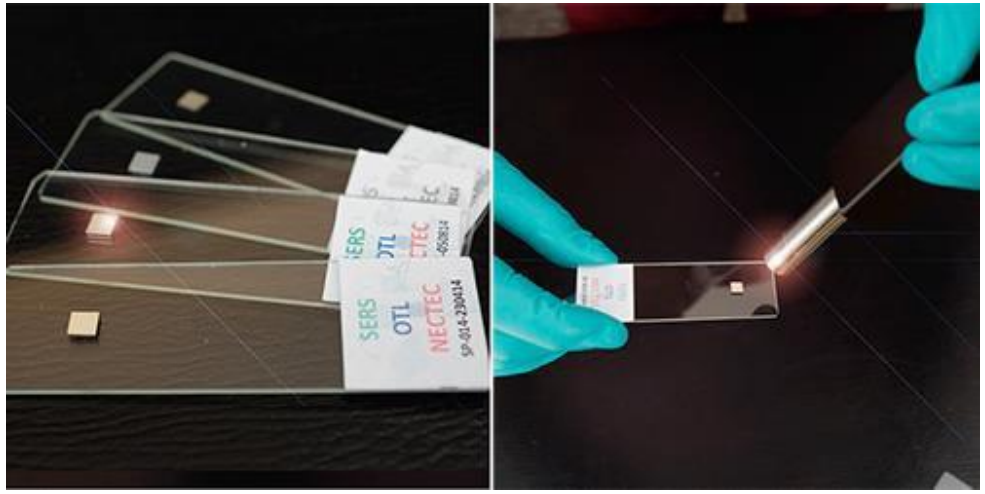
Substrates – Nanogaps

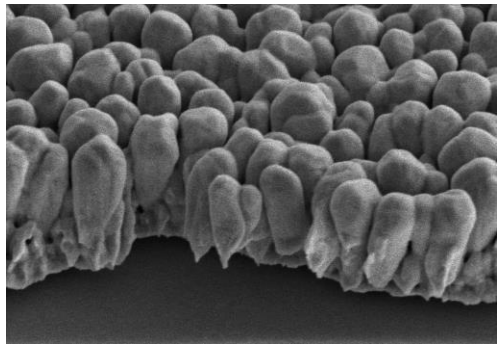
❖ Detection of drugs using SERS - Coworks with Metrohm Raman (Keith Carron)



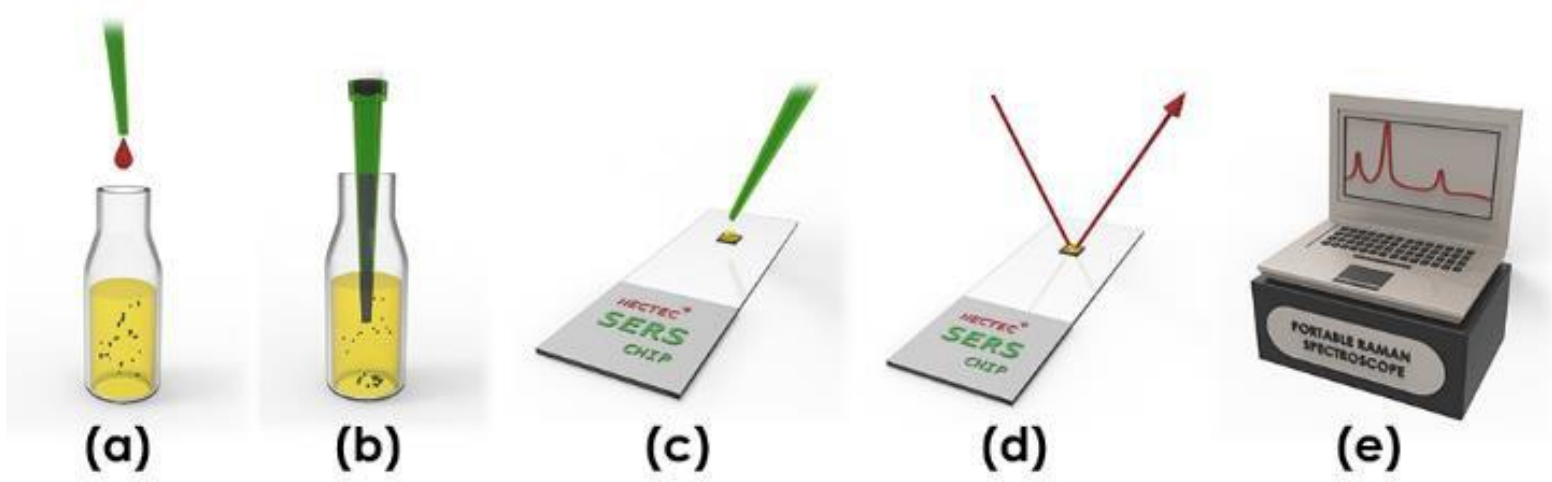
Substrates – Nanogaps

Brand Name:	OnSpec (NecTec)
Type:	Film-based
Material:	Silver nanorods
Prep. Technique:	Physical vapor deposition – Sputtering
Spec.:	Compatible with all Raman spectroscopes Compatible with 785nm laser
Features:	High sensitivity for trace detections of chemical molecules

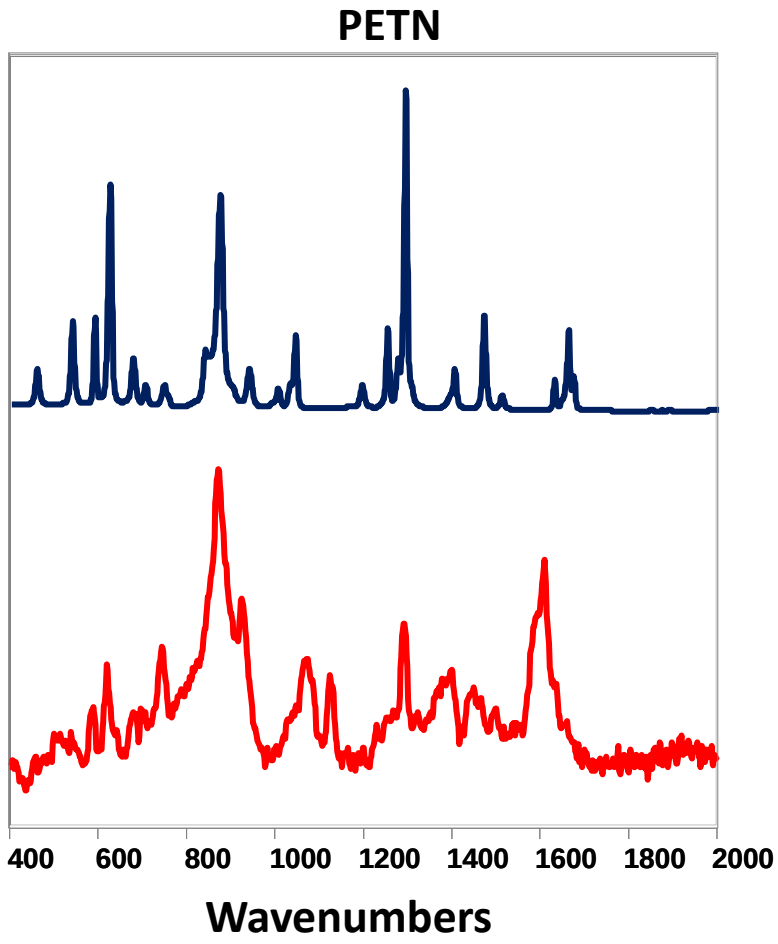




Substrates – Nanogaps



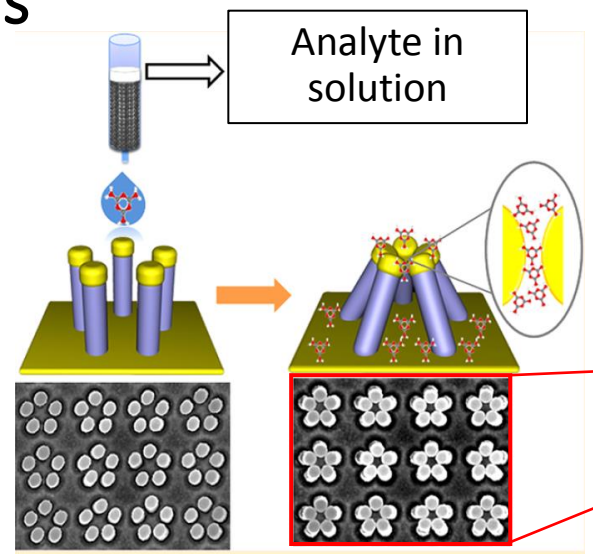
(a) prepare samples in diluting agent
(b) sampling
(c) drop on the SERS chip
(d) collect Raman data
(e) analyses

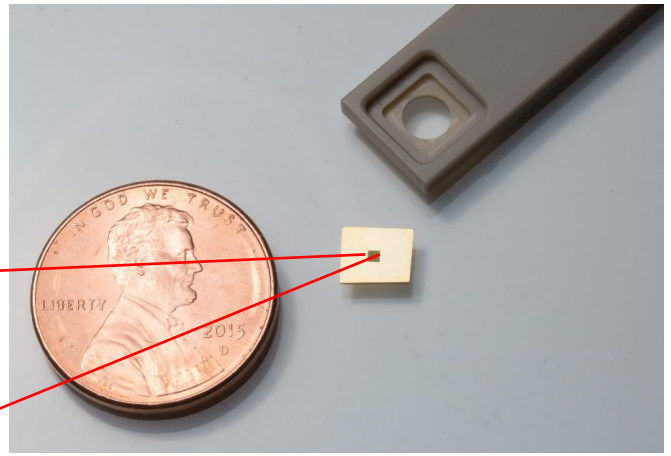


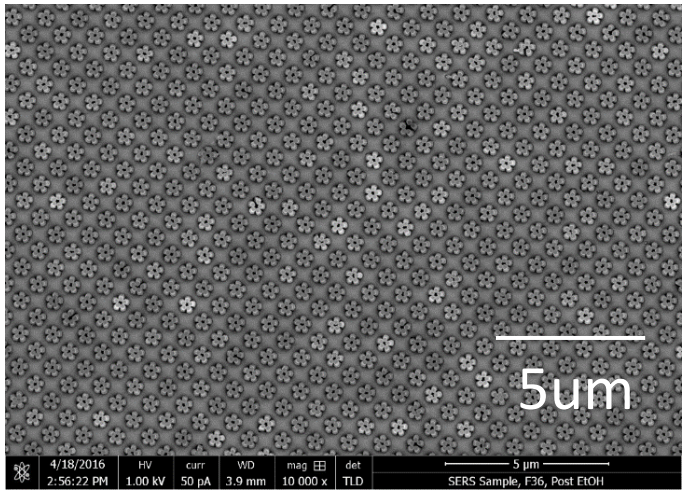
Substrates – Nanogaps

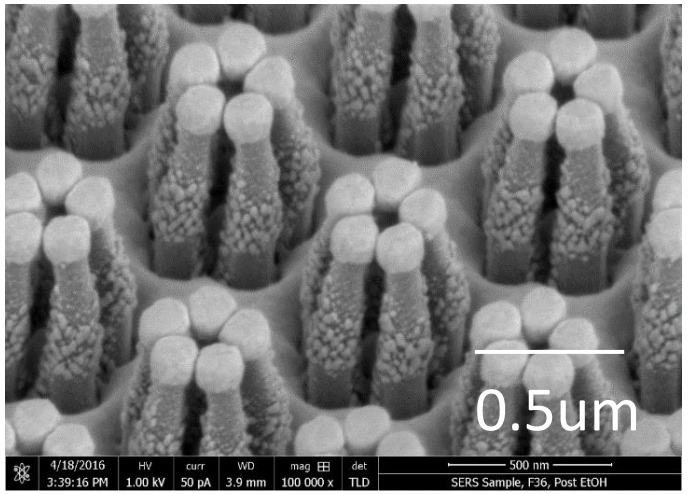
HP SERS Sensors

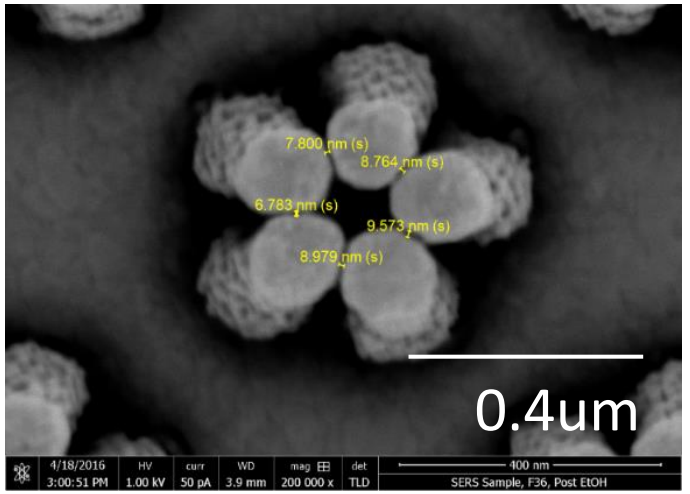
dx.doi.org/10.1021/ja105248h | *J. Am. Chem. Soc.*, 2010, 132, 12820–12822
dx.doi.org/10.1021/ja200247x | *J. Am. Chem. Soc.*, 2011, *133* (21), pp 8234–8239
dx.doi.org/10.1021/ac302025q | *Anal. Chem.* 2012, 84, 9303−9309





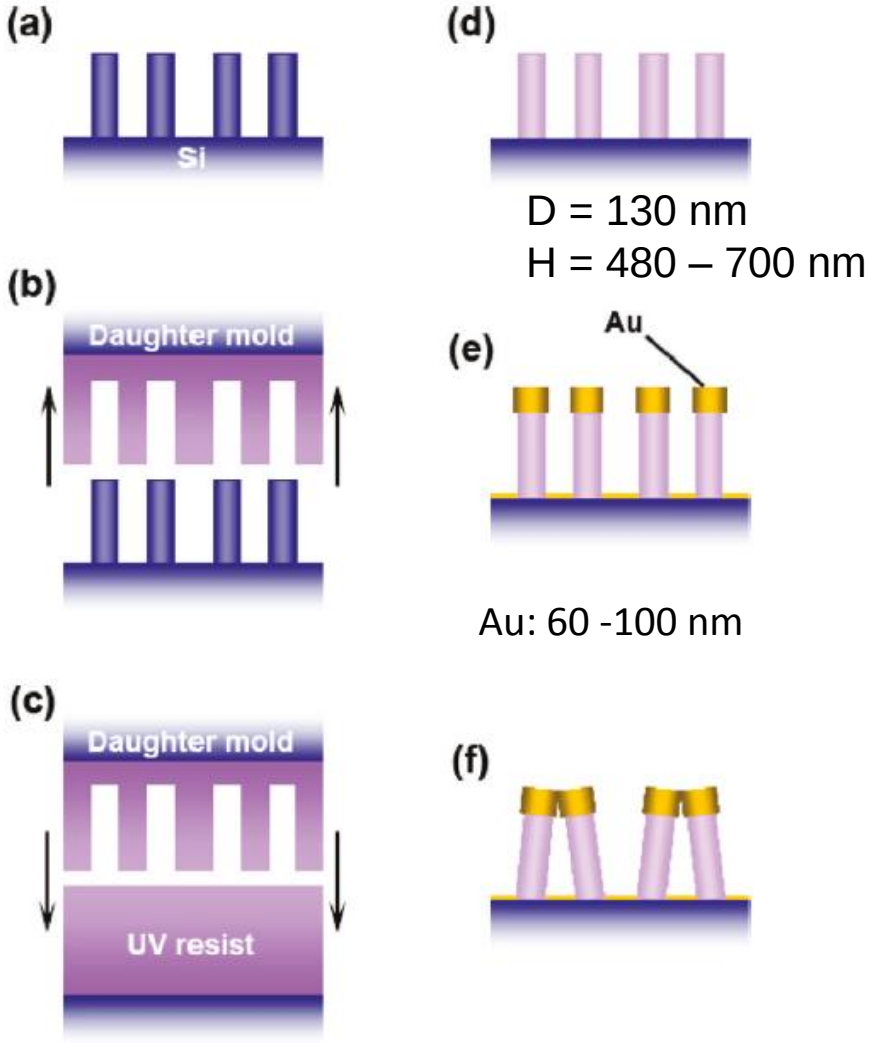






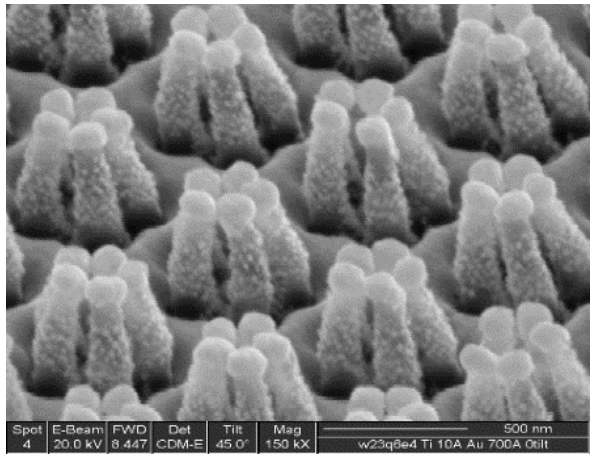
Substrates – Nanogaps

Sensor fabrication – rigid and flexible nanoimprint lithography



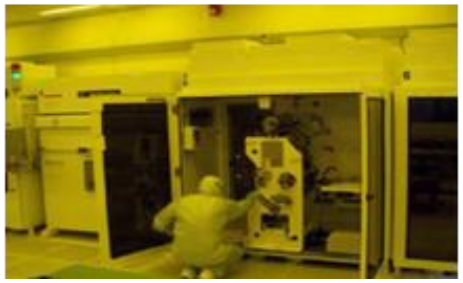
D = 130 nm
H = 480 – 700 nm

Au: 60 -100 nm

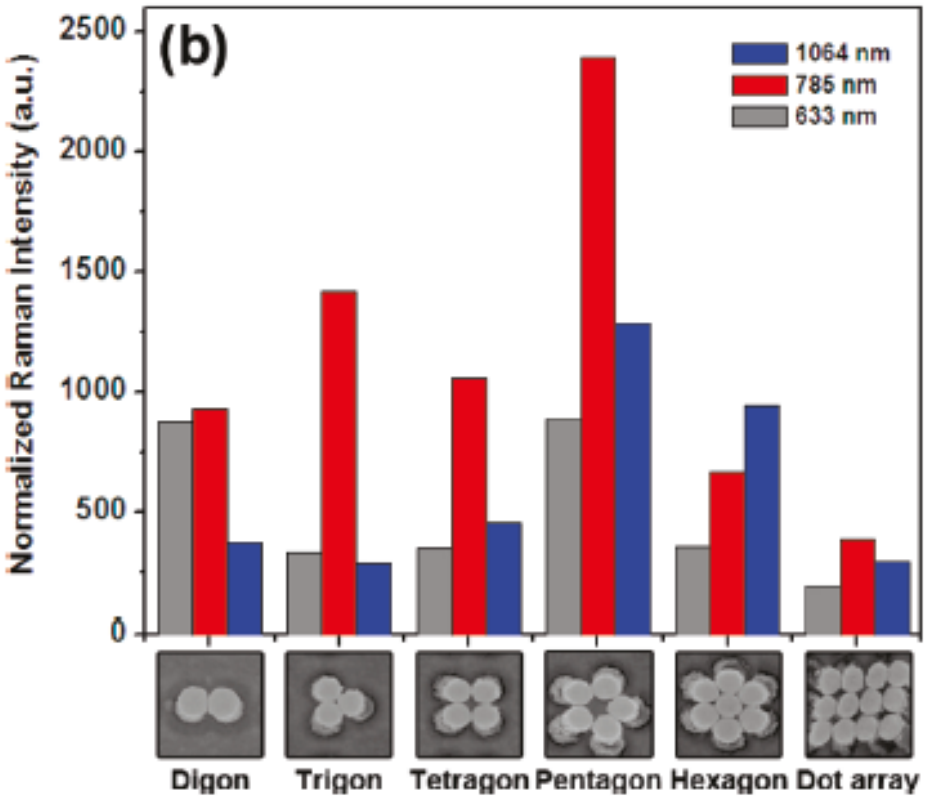


Imprint on 8 inch wafer

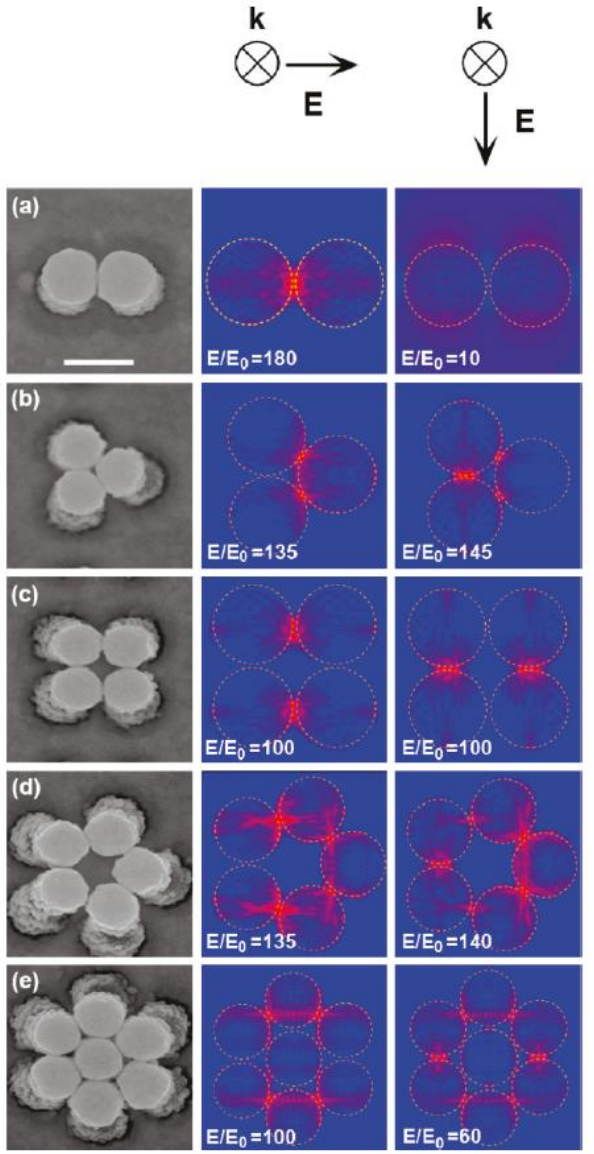
Roll-to-roll



Hot-spot engineering in polygonal nanofinger assemblies

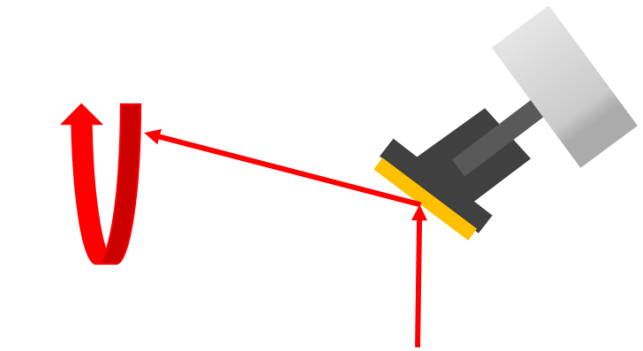


dx.doi.org/10.1021/nl201212n | *Nano Lett., 2011, 11 (6), pp 2538–2542*

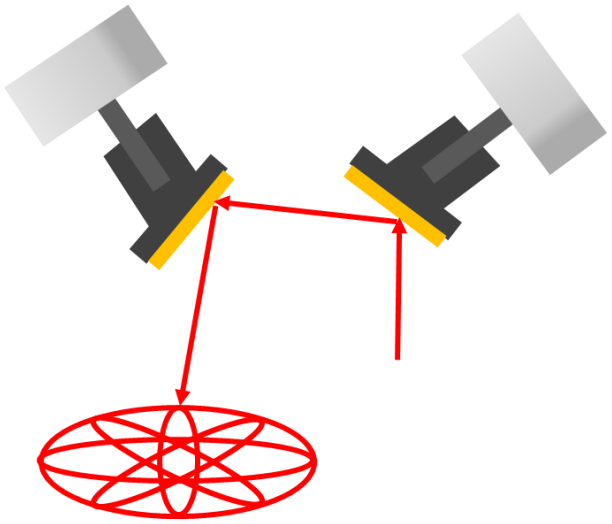


Methods Orbital Raster Scan (ORS)

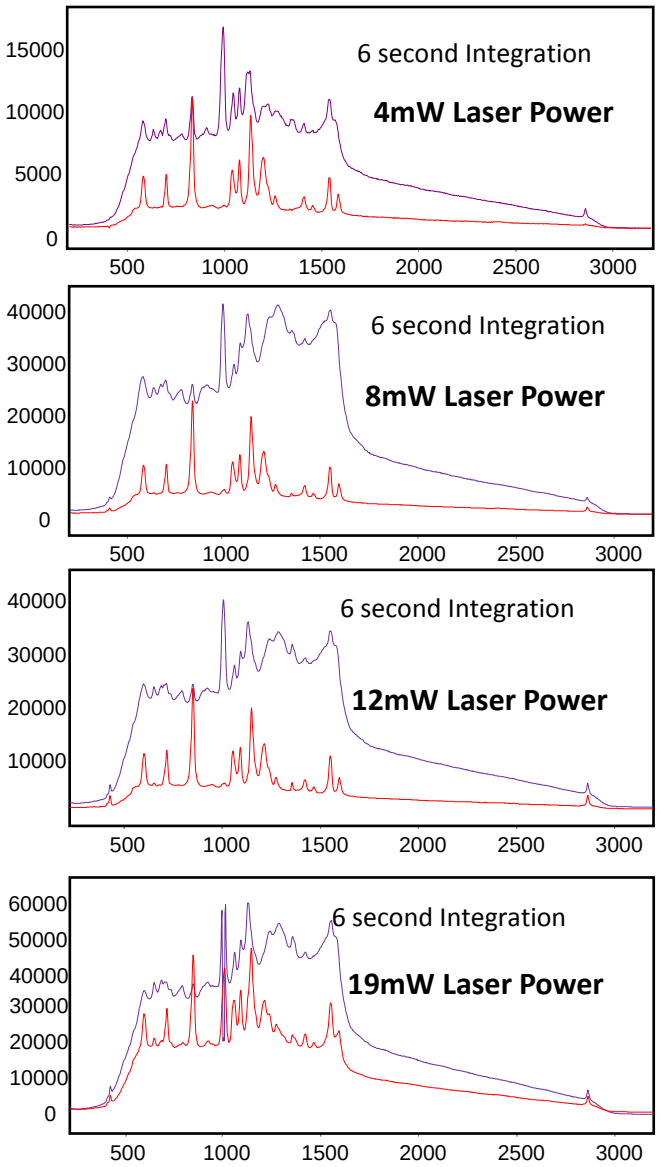
SERS is sensitive to laser heating. ORS is a good way to prevent sample damage.



One-Dimensional



Two-Dimensional



Methods Orbital Raster Scan (ORS)

Problem:

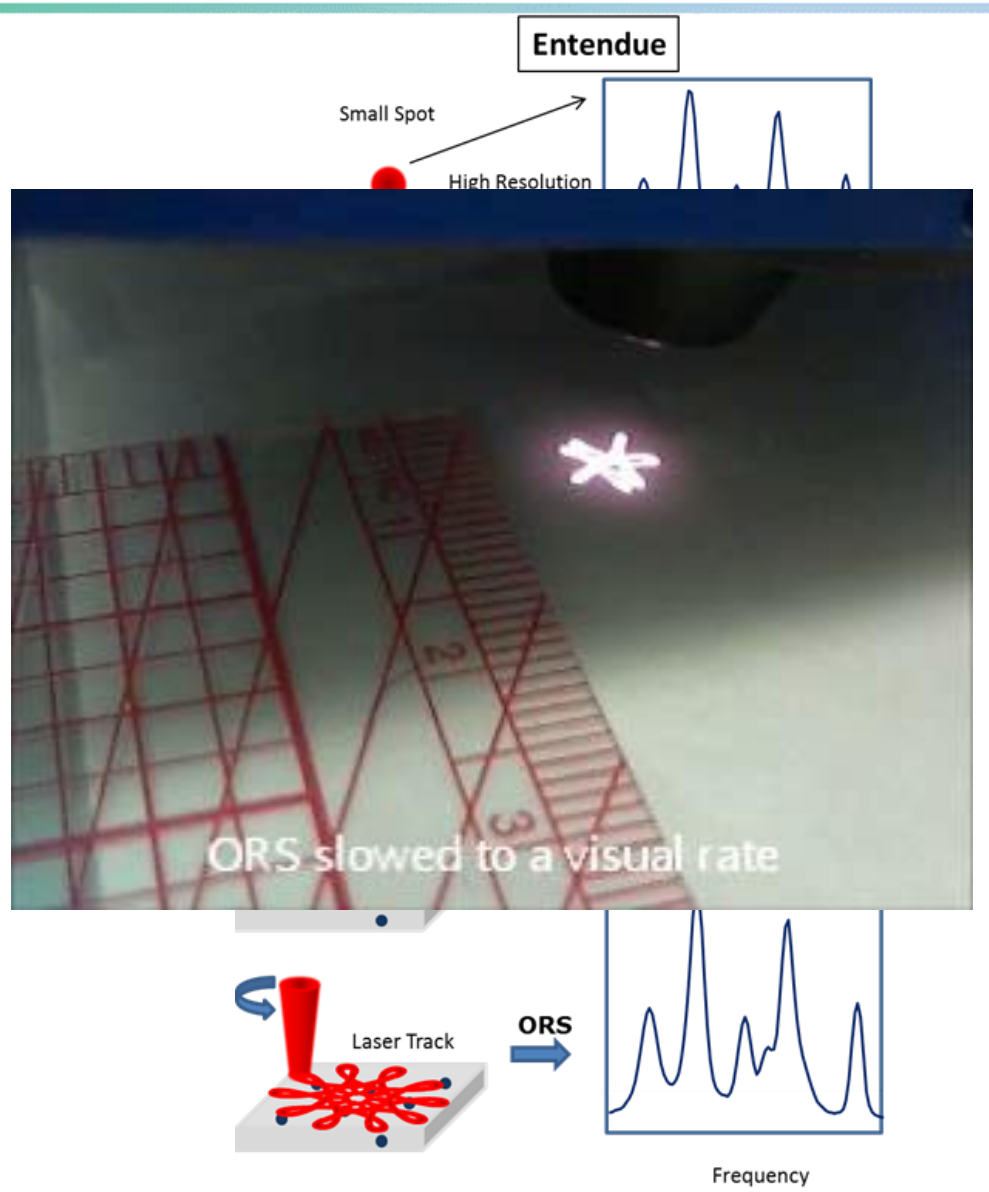
As Raman instruments shrink they container shorter focal length spectrographs.

$\Delta\lambda = wd\cos(\theta)/\mathbf{F}$ **(Spectral Resolution)**

$2w_0 = (4\lambda/\pi)^* \mathbf{F}/D$ **(Laser Spots Size)**

Small spot size causes problems with detection:

- Poor spatial averaging of heterogeneous samples
- Burning of samples due to high laser intensity



Methods Dynamic Raman Scattering

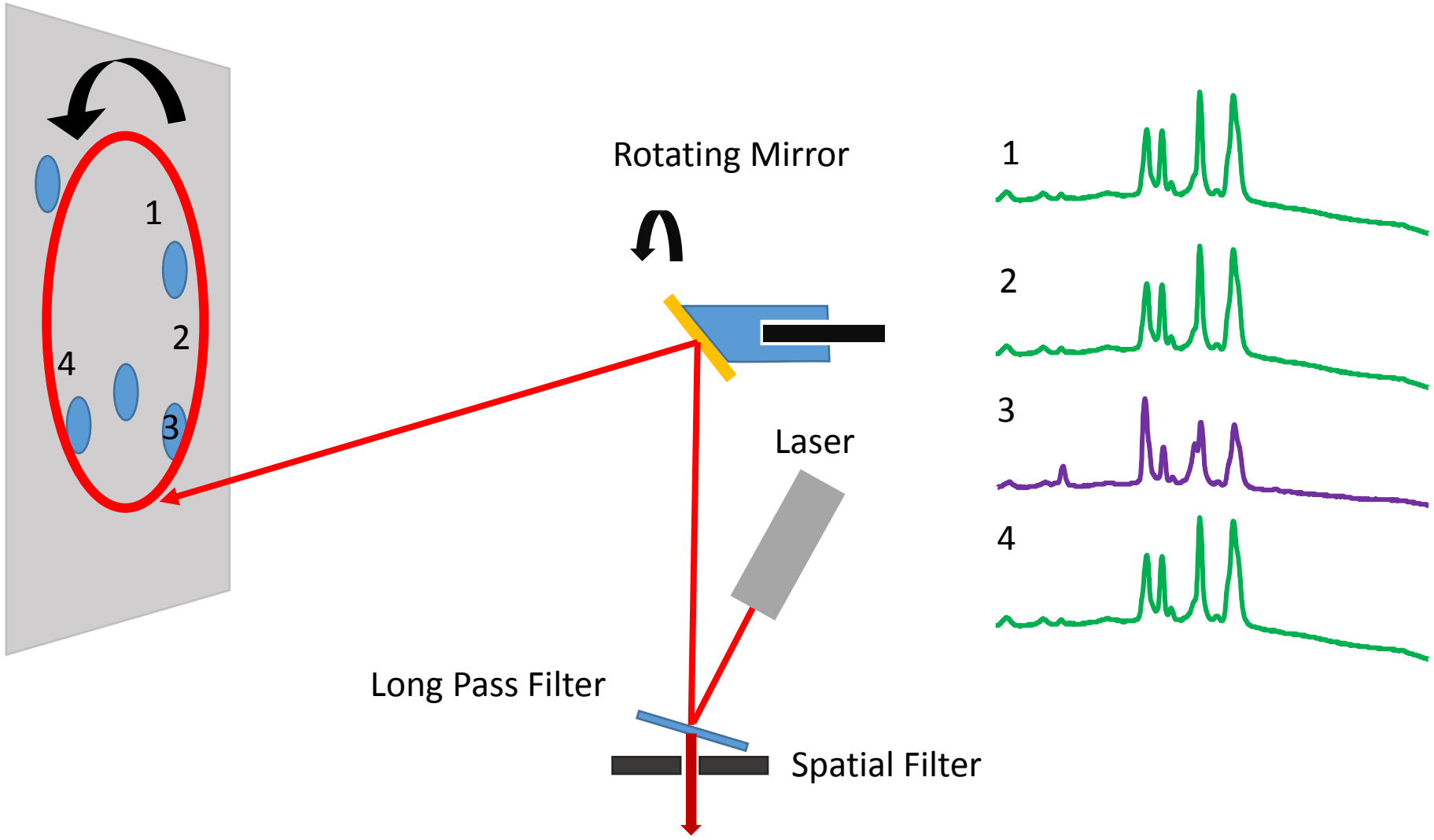
ORS + DRS

Search and Find Functionality

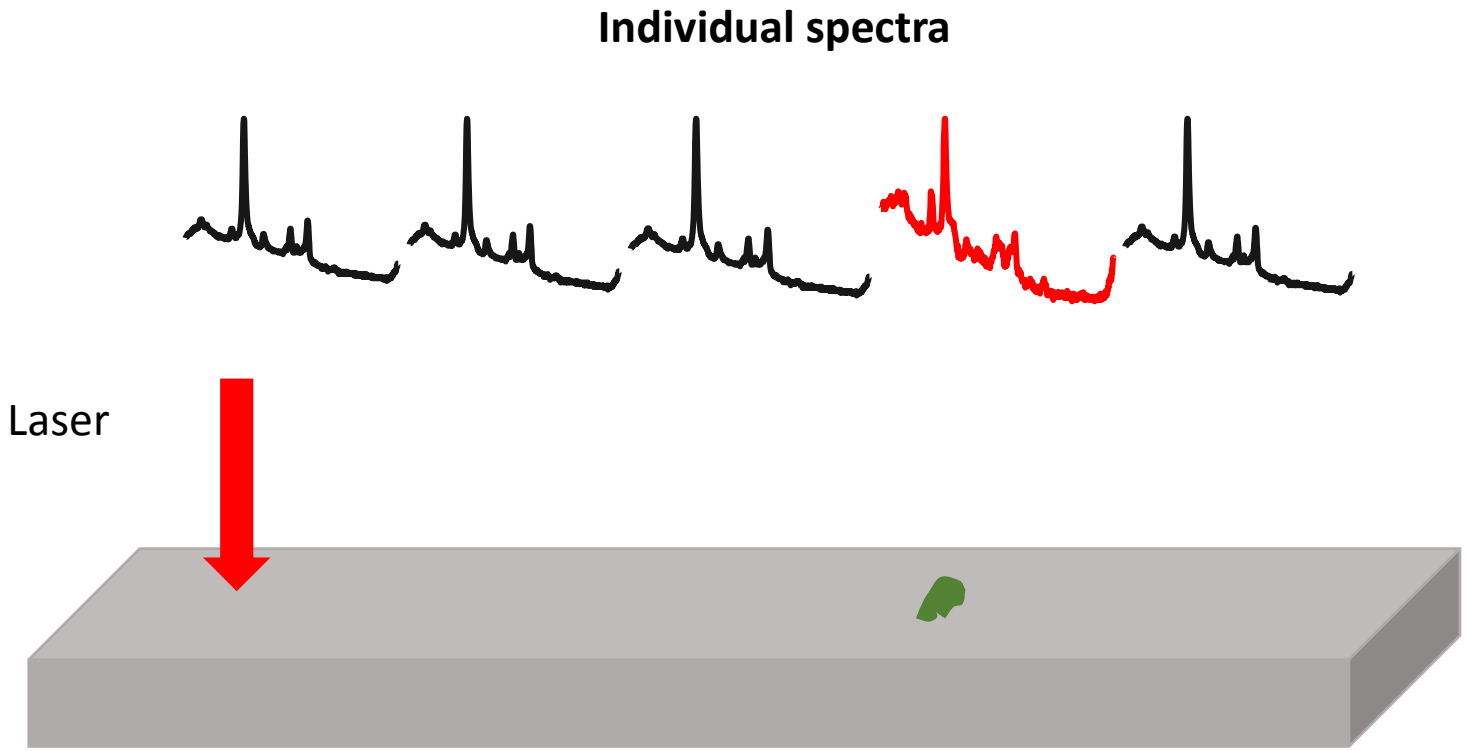
- **ORS to step through an area**
- **Algorithms to analyze data**
- **Precision motors to return to regions of interest**

Methods Dynamic Raman Scattering

2-Dimenional Sample

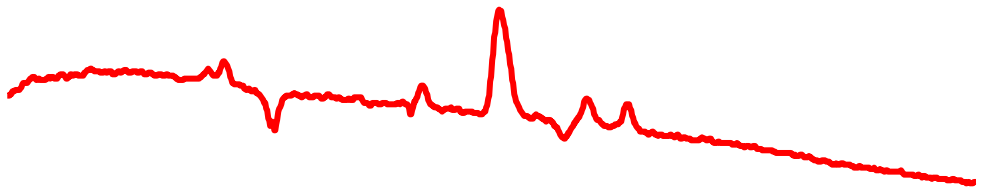


Methods Dynamic Raman Scattering



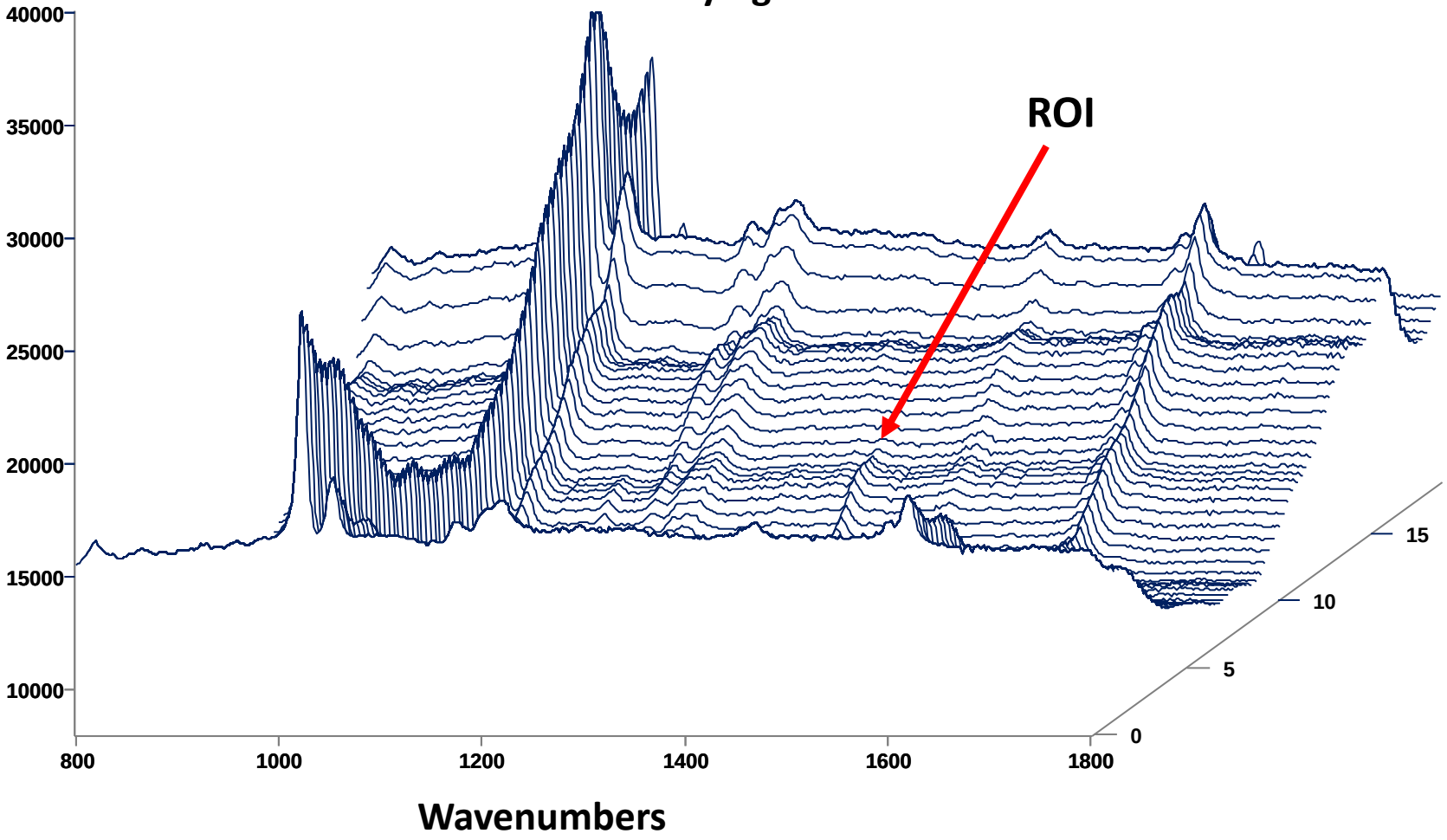
As the laser moves it take multiple acquisitions across the surface. The unit spectral features for individual components of a mixture can be extracted.

Extracted target mixture component with DRS

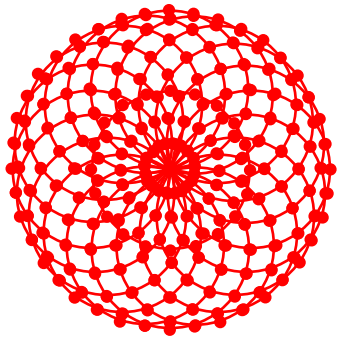


Methods Dynamic Raman Scattering

Studying Filters for “unknown materials”



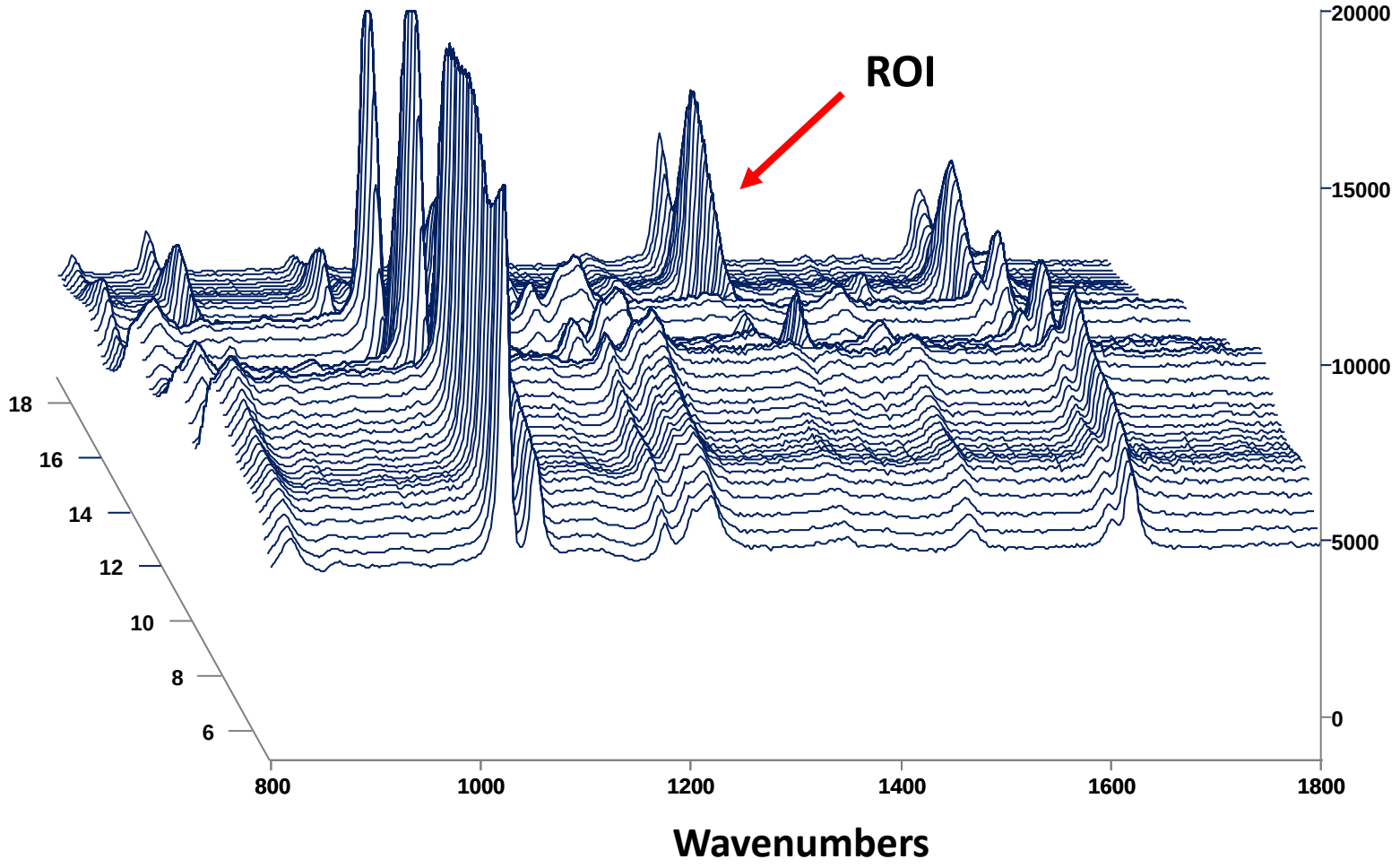
Macro-Search reports regions of interest



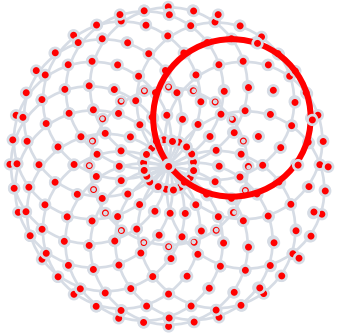
Methods Dynamic Raman Scattering

Metrohm Raman

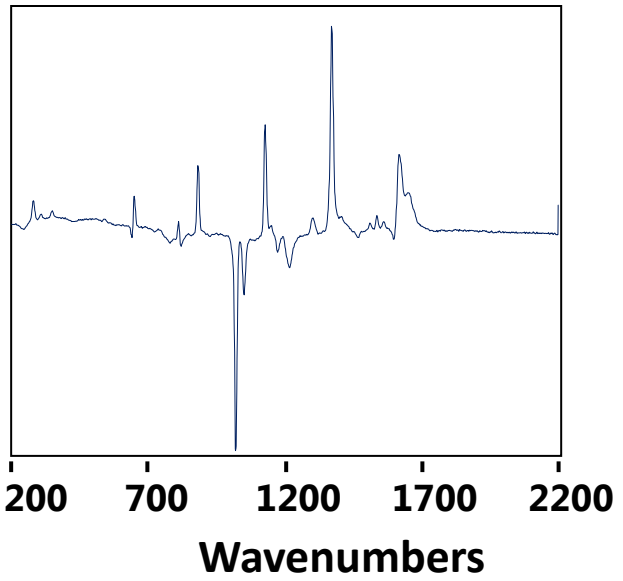
Studying Filters for “unknown materials”



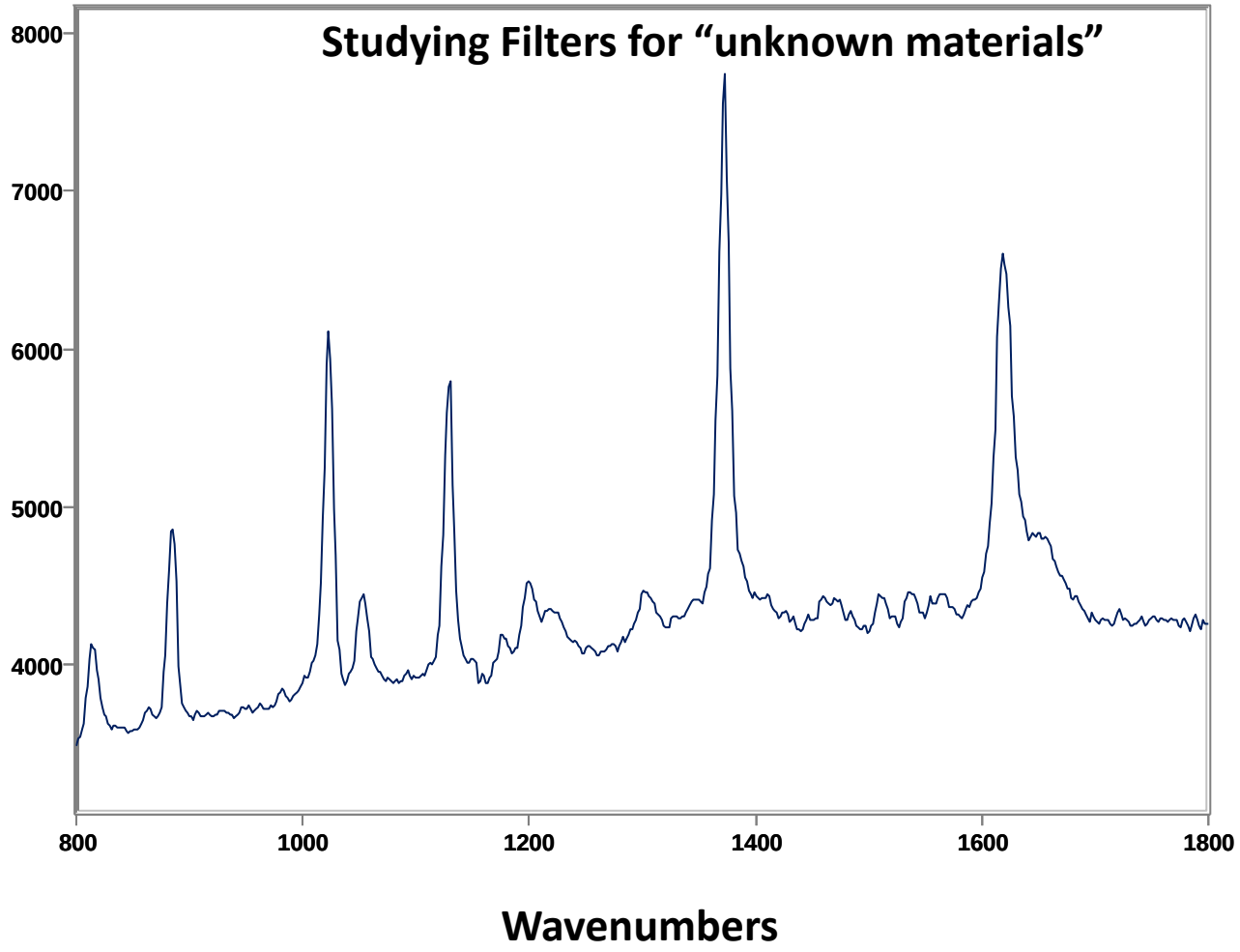
Micro-Search and Identification



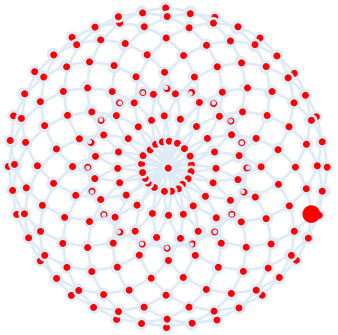
DRS



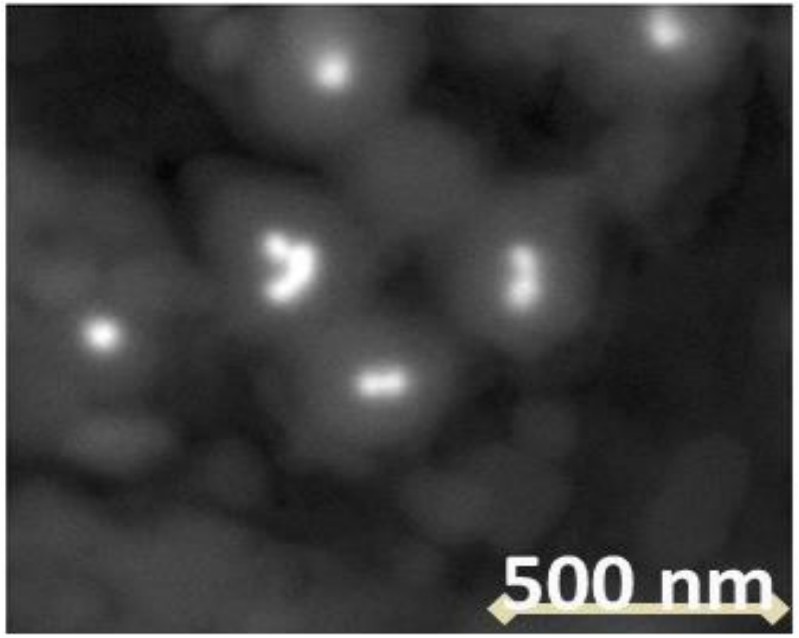
Methods Dynamic Raman Scattering

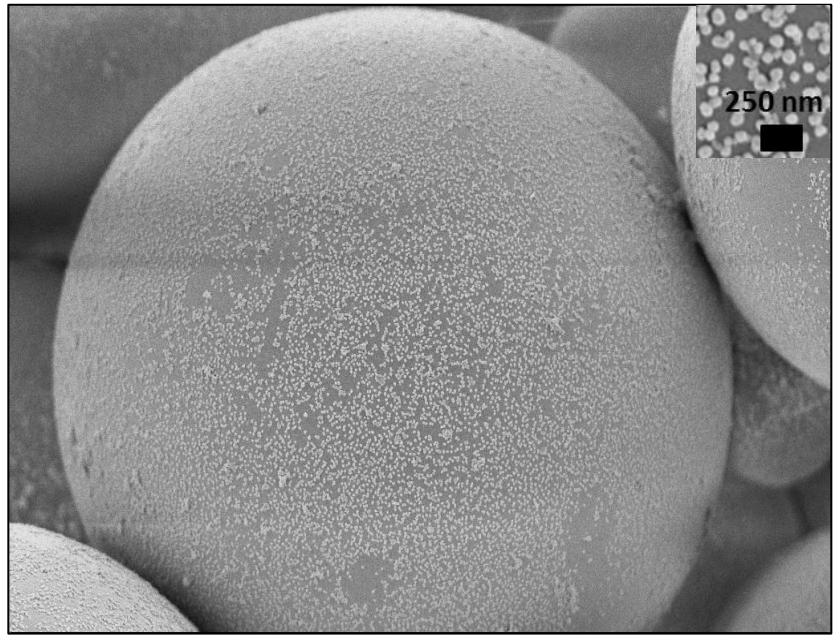


Return for long analysis - identification

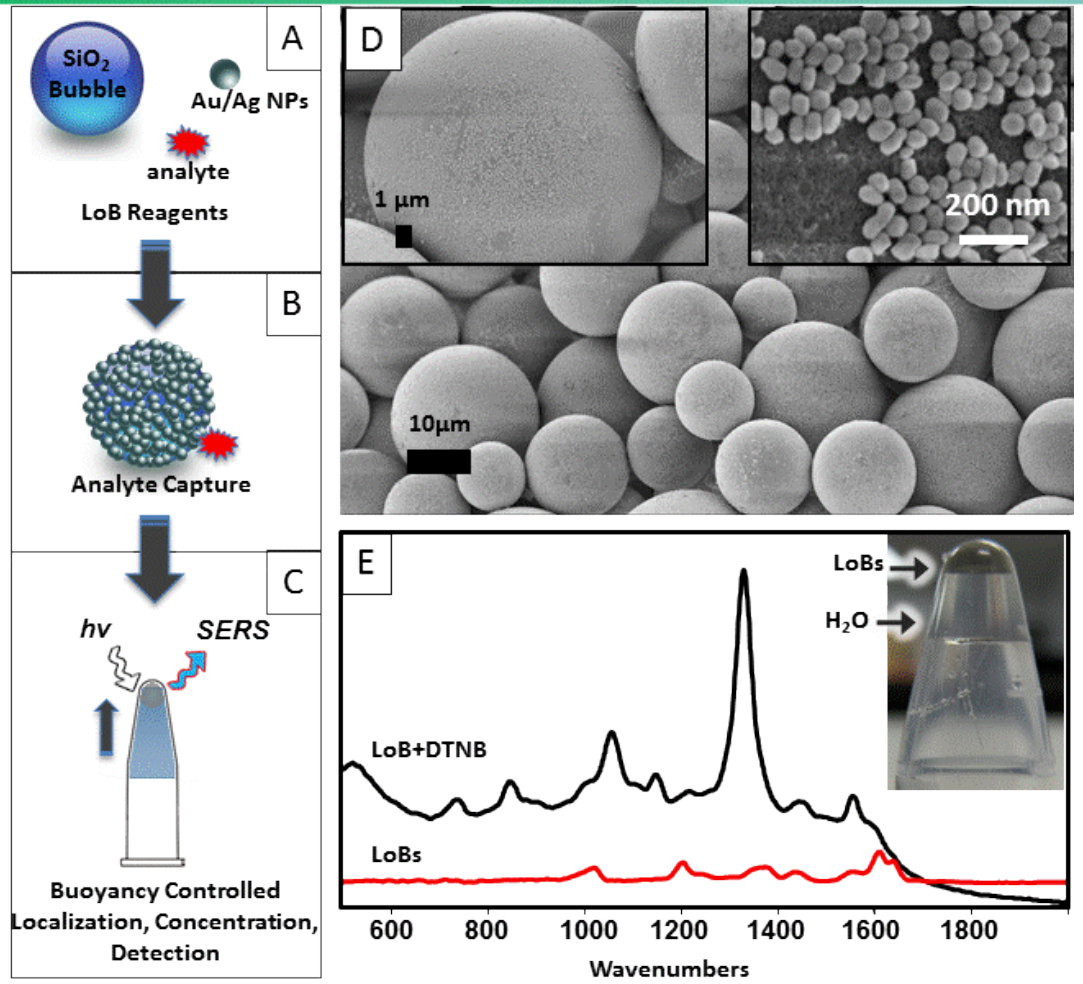


Methods Buoyant Separation





Methods Buoyant Separation



Left, concept for LoB direct assay in solution. This direct assay uses the SERS coated LoB to couple the analyte. Results from an DTNB test showing the extraction and concentration of the analyte on the surface of the LoB.

Lab-on-a-Bubble (LoB): Synthesis, Characterization and Evaluation of Buoyant Gold Nanoparticle-Coated Silica Spheres; Schmit, V.; Martoglio, R.; Scott, B.; Strickland, A.; Carron, K., J. Am. Chem. Soc. **2012**, 134, 59−62,

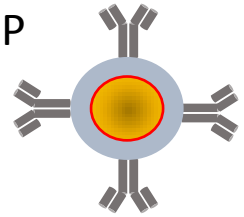
Buoyant Separation of SERS signals

Indirect Assays -- Cholera Toxin Example

Metrohm Raman

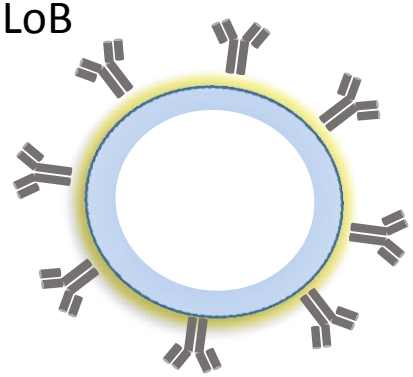
Components

AuNP

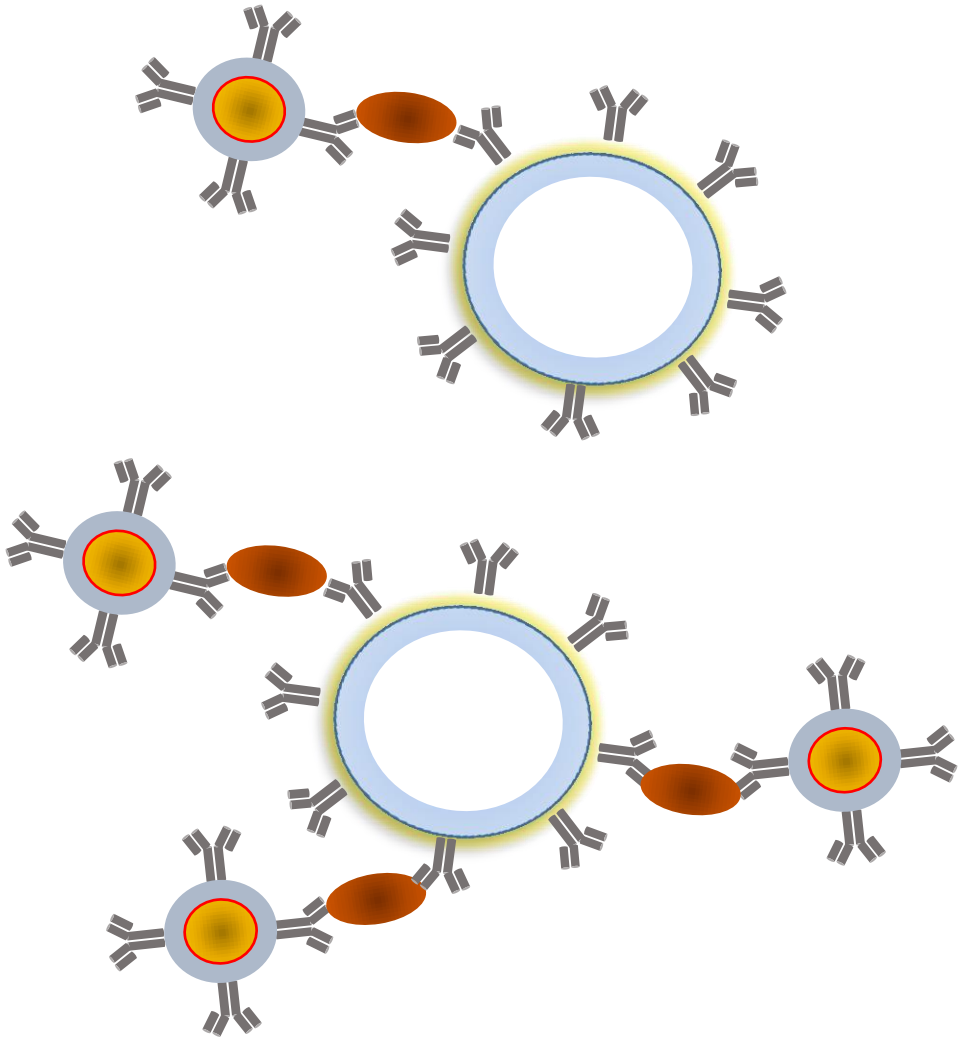


CT-AG

LoB

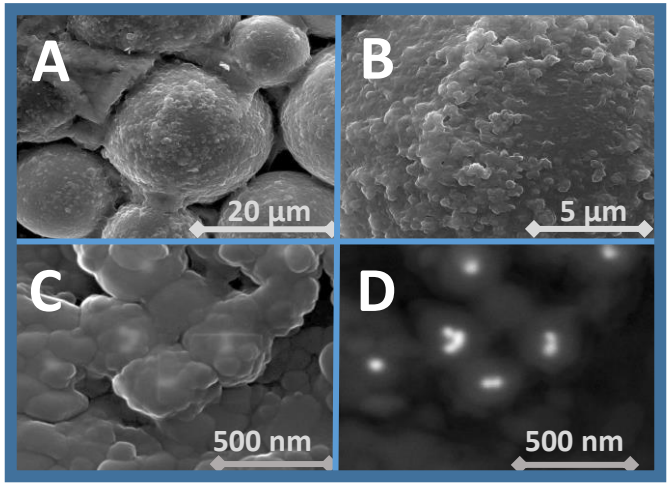


Results

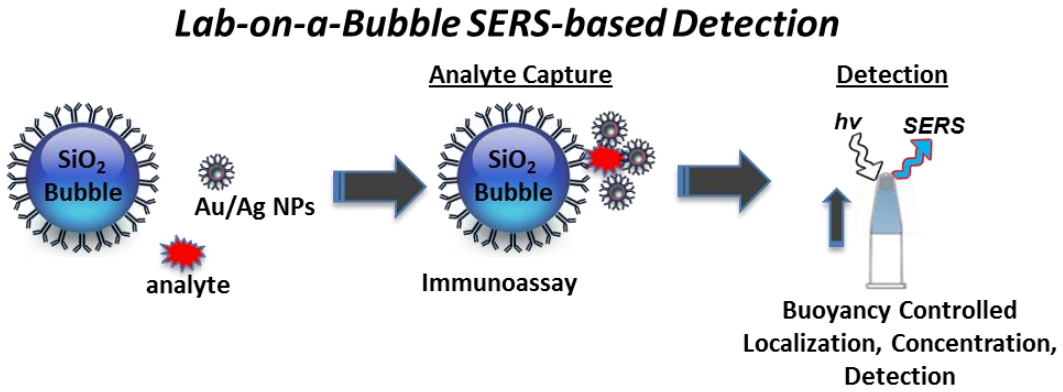


Methods Buoyant Separation

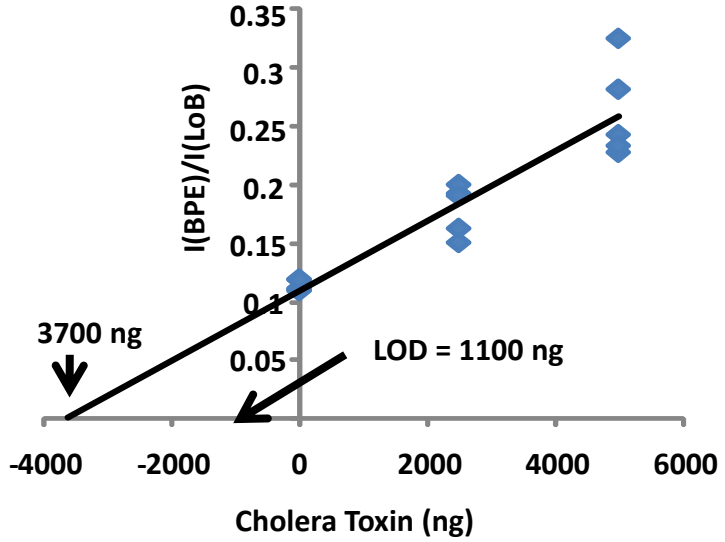
SEM Images



Graphic Representation



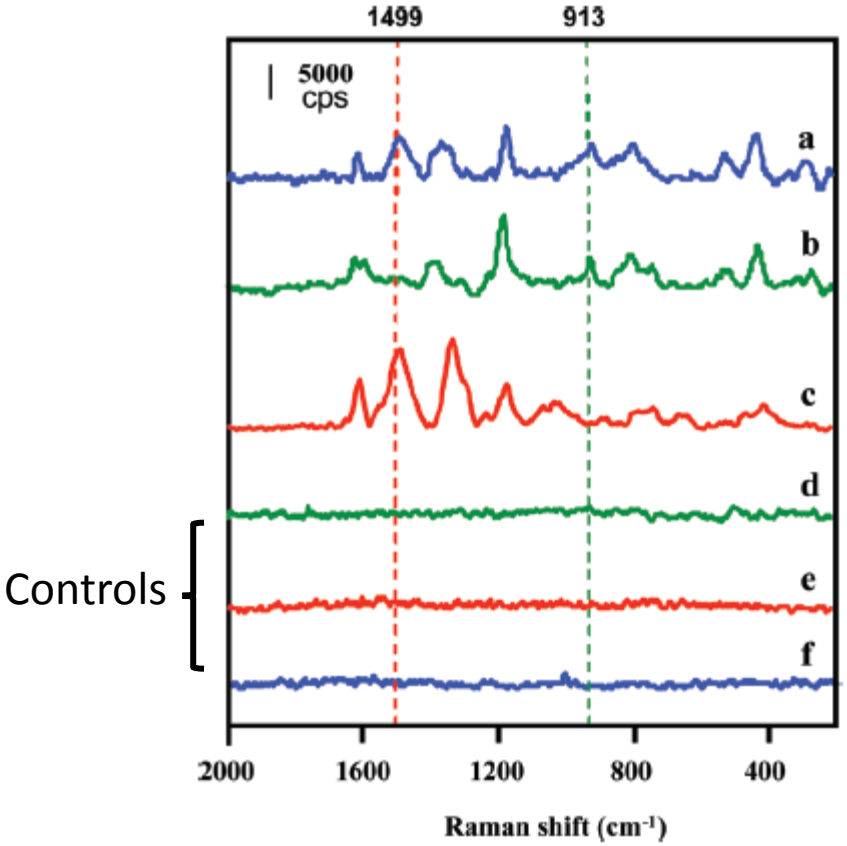
Above, concept for LoB biological assay. This indirect assay uses the analyte to couple the LoB particle and the nanoparticle reporter. Right, results from an assay for Cholera toxin. Note, the LOD is independent of the volume. LoB assays are mass detection, not concentration.



Lab-on-a-Bubble Surface Enhanced Raman Indirect Immunoassay for Cholera; Schmit, K., Martoglio, R., Carron, K.,, *Anal. Chem.*, **2012**, *84* (9), pp 4233–4236

Methods Paramagnetic Separation

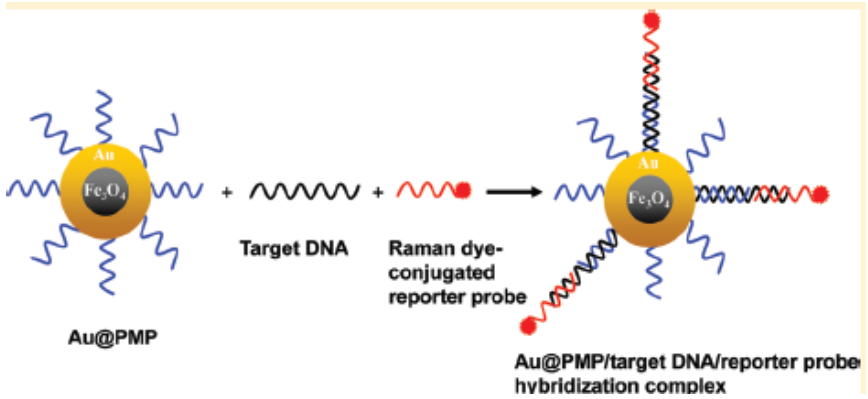
Multiplex Paramagnetic DNA Assay



Rift Valley Fever Virus + West Nile Virus

Rift Valley Fever Virus

West Nile Virus



Surface-Enhanced Raman Scattering Detection of DNAs Derived from Virus Genomes Using Au-Coated Paramagnetic Nanoparticles, Zhang, Harpster, Wilson, Johnson; Langmuir, 2012.

Methods Tags

Michael Natan (Van Duyne Postdoc 1988)

Started S evelop at Penn State as ociate Professor and left x. Nanoplex was sold Oxonica was sold to C rte is SERS material.

By far the most successful is the SERS Reporter. This robust nanoparticles have a noble metal core, a Raman label, and a silica coating.

They are:

- Robust
- Bright
- Non-bleaching
- Multiplexed

Langmuir **2003**, *19*, 4784−4790

Glass-Coated, Analyte-Tagged Nanoparticles: A New Tagging System Based on Detection with Surface-Enhanced Raman Scattering

Shawn P. Mulvaney,*,† Michael D. Musick,† Christine D. Keating,† and Michael J. Natan‡

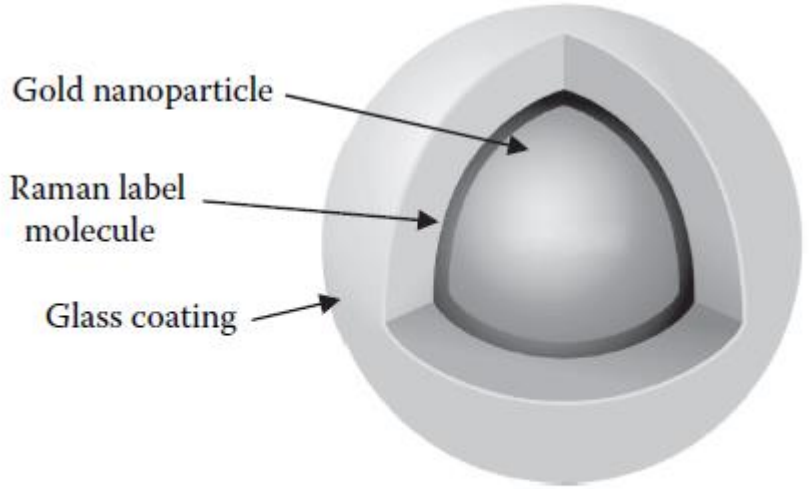
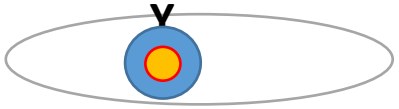


FIGURE 4.1 Cartoon showing architecture of Nanoplex Biotags.

Methods Tags



Reagent Pad with Natan's Reporters

LFI – Lateral Flow Immunoassay

WO 2007/090058

PCT/US2007/061136

LATERAL FLOW IMUNOASSAY WITH ENCAPSULATED DETECTION MODALITY

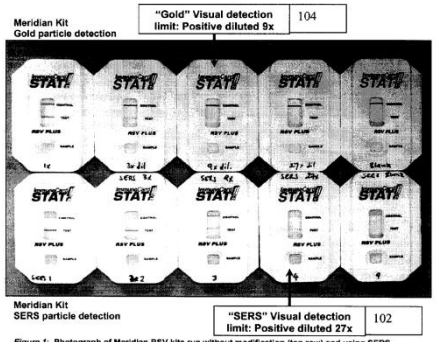
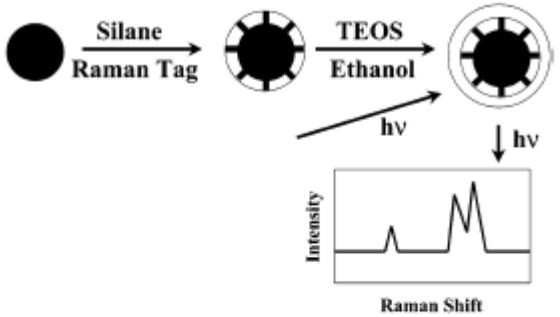
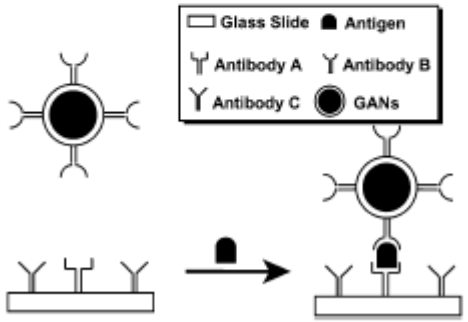


Figure 1: Photograph of Meridian RSV kits run without modification (top row) and using SERS nanotags as the detection modality (bottom row). From left to right, samples were run using a positive control followed by 3-fold serial dilutions and compared to a blank at the far right.

Scheme 1. Cartoon of GAN Synthesis and Spectral Activity



Scheme 2. Cartoon Depicting the Use of GANs To Label an Immunoassay[a]



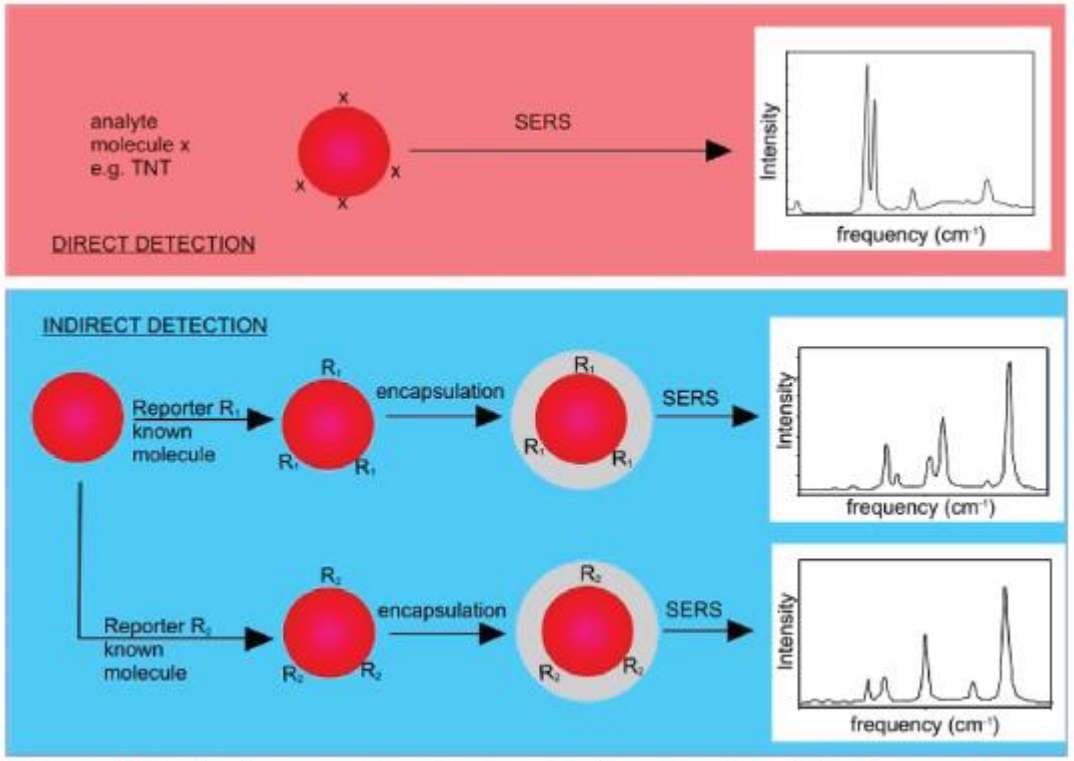
[a] The antigen is identified by the Raman spectrum of the attached GAN label.

Methods Tags

Surface-Enhanced Raman Spectroscopy and Homeland Security: A Perfect Match?

Rebecca S. Golightly,[†] William E. Doering,[†] and Michael J. Natan*

Oneida Materials Inc., 125 East Middlefield Road, Mountain View, California 94043. [†]These authors contributed equally to this work.



Scheme 1. Illustration demonstrating methods used for direct detection *via* SERS (top panel) and preparation of labels for SERS-based indirect detection (bottom panel).

	1 Component Tags	2 Component Tags	3 Component Tags
$\frac{n!}{k(k-n)!}$	10	45	120
$L = 2^n - 1 = 1023$ Total tags from 10 unique compounds			
[n] = number of unique compounds [k] = number of compounds in use [L] = total number of unique tags			

Conclusion

1. SERS works! It is a viable method to convert medium sensitivity Raman spectroscopy into a trace technique.
2. The current prices range from ~$5 to $30. But the cost is scalable with the volume of materials. It will decrease.

3. Liquid colloidal solutions can be dispensed as liquids which is useful in some applications
   - Stability is always a concern
4. Deposited nanoparticles solve much of the stability problems and create low cost SERS materials
   - Sensitivity of these materials is lower due to the 3-dimensional matrix and the particles have a coating from the reduction process.
5. Plasmonic materials can be tuned to a particular laser excitation through distance between the nanofeatures
   - The are made with deposited bare metals that can be more reactive than deposited nanoparticles
   - Their fabrication can be expensive
6. Nanogap materials use the high electric fields between nanoparticles and have bare metal surfaces
   - These are more expensive that deposited nanoparticles
   - These exhibit high sensitivity from the bare metal surface and may be scalable to bring the cost down
7. Coated nanoparticles can be used as very bright tags for biological assays and anti-counterfeiting

Acknowledgements

Jason Guicheteau, Ewelina Glinka-Lewis and NATO for organizing this conference.

Diagnostic anSERS (Wei Yu)
Ocean Optics (D
iFyber (Aaron S
KimStrates (Dor
Renishaw Diagr
Dstl (Neil Shanc
OnSpec (Kaowti
HP (Anita Rogac
Michal Natan

Metrohm Rama
Bryan Ray
Shane Buller
Mark Watson