Fiber SERS Sensors for Molecular Detection

Claire Gu

Department of Electrical Engineering, University of California, Santa Cruz, CA 95064, USA

Multidisciplinary Collaborations

- Collaborators and Students
  - Xuan Yang, Yi Zhang, Chao Shi, He Yan, Chao Lu, Kazuki Tanaka, Prof. Bin Chen (EE)
  - Adam M. Schwartzberg, Leo Seballos, Rebecca Newhouse, Tammy Olson, Damon A. Wheeler, Debraj Ghosh, Lei Tian, Qiao Xu, Alissa Y. Zhang, Dr. Fang Qian, Prof. Shaowei Chen, Prof. Yat Li, Prof. Jin Z. Zhang (Chemistry)
  - Prof. Liangcai Cao, and Zhigang Zhao ,Yuan Yao, Jiatao Zhang, Prof. Changxi Yang, Prof. Guofan Jin (Tsinghua University, Beijing, China)
  - Dr. Tiziana C. Bond (LLNL)

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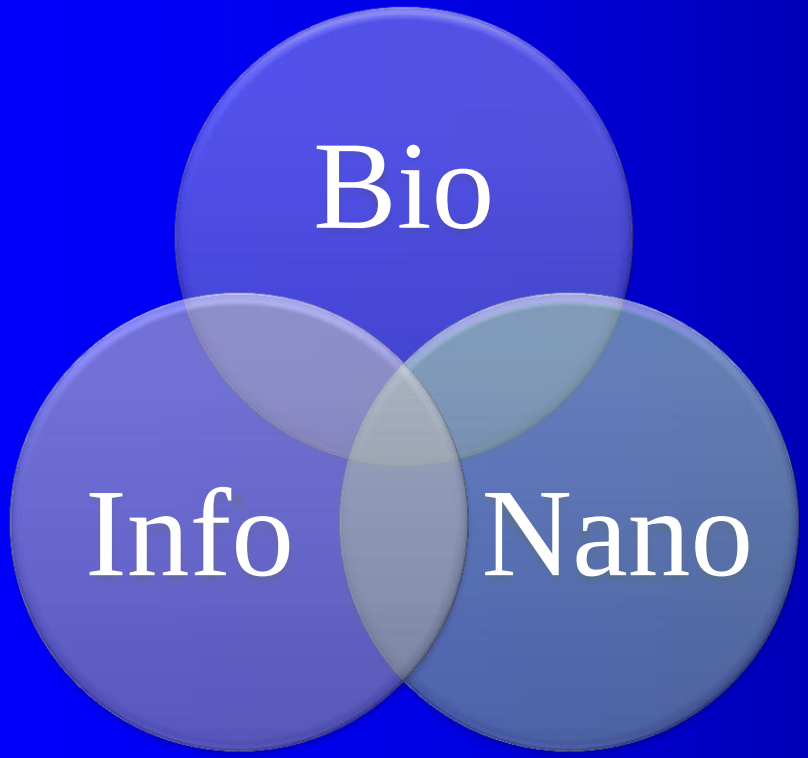
Outline

- Introduction and Motivation
- SERS Substrate
  - Au or Ag nanoparticle aggregates
  - Chemistry and SERS study
- Fiber-SERS Sensor
  - Molecular specificity & extremely high sensitivity
  - Chemical and biomedical applications
- Optical Fibers as a Platform for Chemical Sensors
  - Fibers – additional sensitivity enhancement (beyond interconnects)
  - Tip-Coated Multimode Fibers (TCMMF)
  - Liquid Core Photonic Crystal Fiber (LCPCF)
  - Nanostructured Optical Fiber
  - Integrated Portable Sensor System
  - Chemical, biomedical, and environmental applications
- Conclusions

Frontiers of Science and Engineering



- Bio
  - Biological and biomedical applications
- Nano
  - Nanoparticle surface enhanced Raman scattering
- Info
  - Information detection by fiber-SERS sensors

Motivation-Biomedical Application of Nanomaterials: Cancer Detection (e.g. lung and ovarian)

Some Disturbing Statistics on Cancer

Over 10 million people diagnosed per year
Causes 6 million deaths per year
12% of worldwide deaths
Cancer rate is *increasing*, could be 15 million by 2020

Cancer	New cases (2000)
1. Lung	1,238,861
2. Breast	1,050,346
3. Colorectal	944,717
4. Stomach	876,341
5. Liver	564,336
…	…
15. Kidney	189,077

Biomedical Applications of Nanomaterials: Cancer Cell and Biomarker Detection with PL and SERS

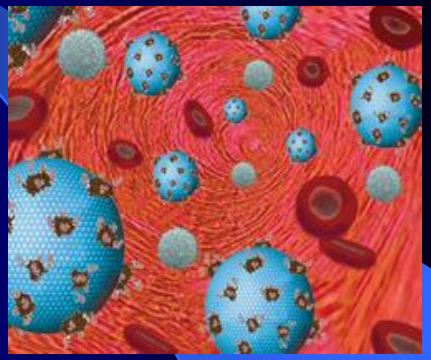
Cancer is one of the most commonly fatal diseases: e.g. lung and ovarian

Early detection is key to survival but challenging

Sensitive detection of cells and biomarkers (antigens, e.g. CA125) with molecular specificity is highly desired

Semiconductor quantum dots (SQD) and metal nanoparticles (MNP) hold great promise for cancer detection

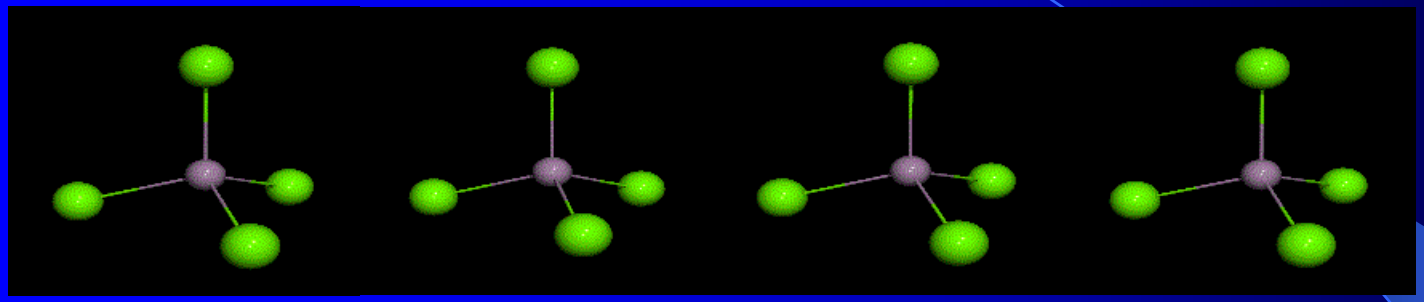
General applications in chemical, biological, and environmental detection

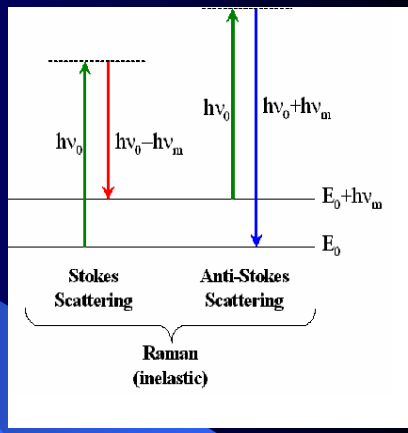


Motivation

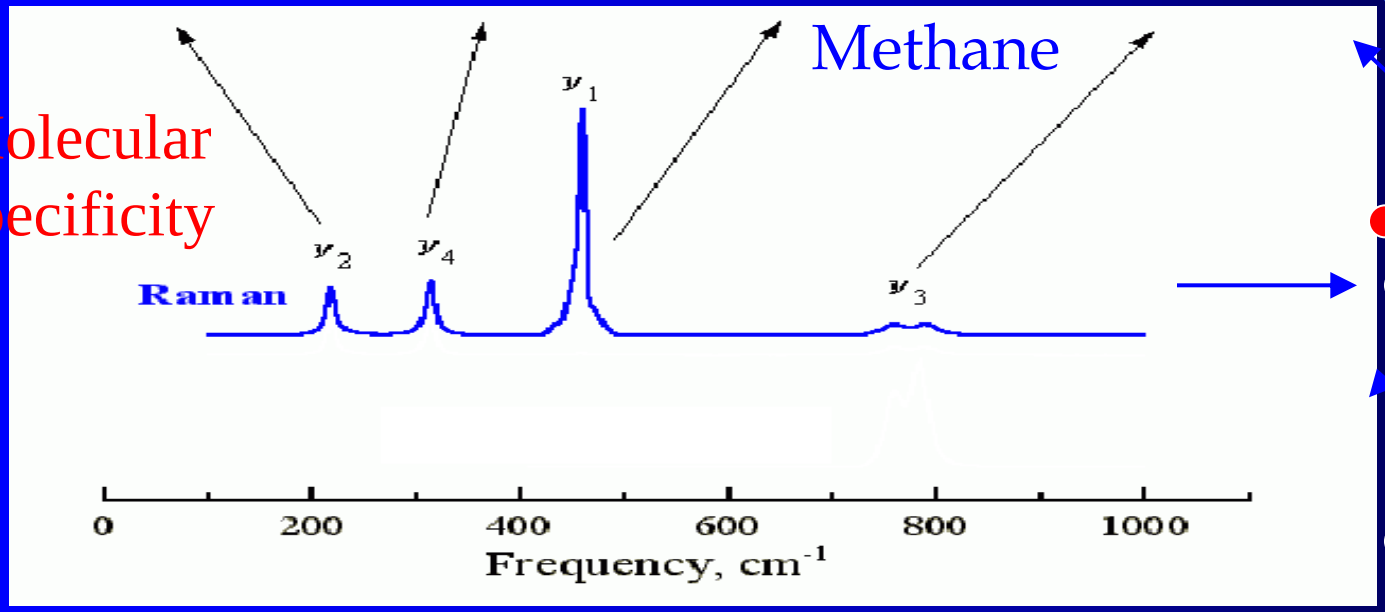
- Environmental
- Medical
- Food and Water Safety
- National Security
- Need a chemical sensor
  - Highly sensitive
  - Molecular specific
  - Flexible and portable
  - Reliable

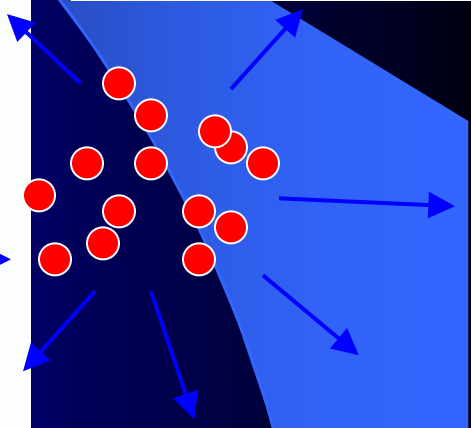
Raman Spectroscopy





Molecular specificity

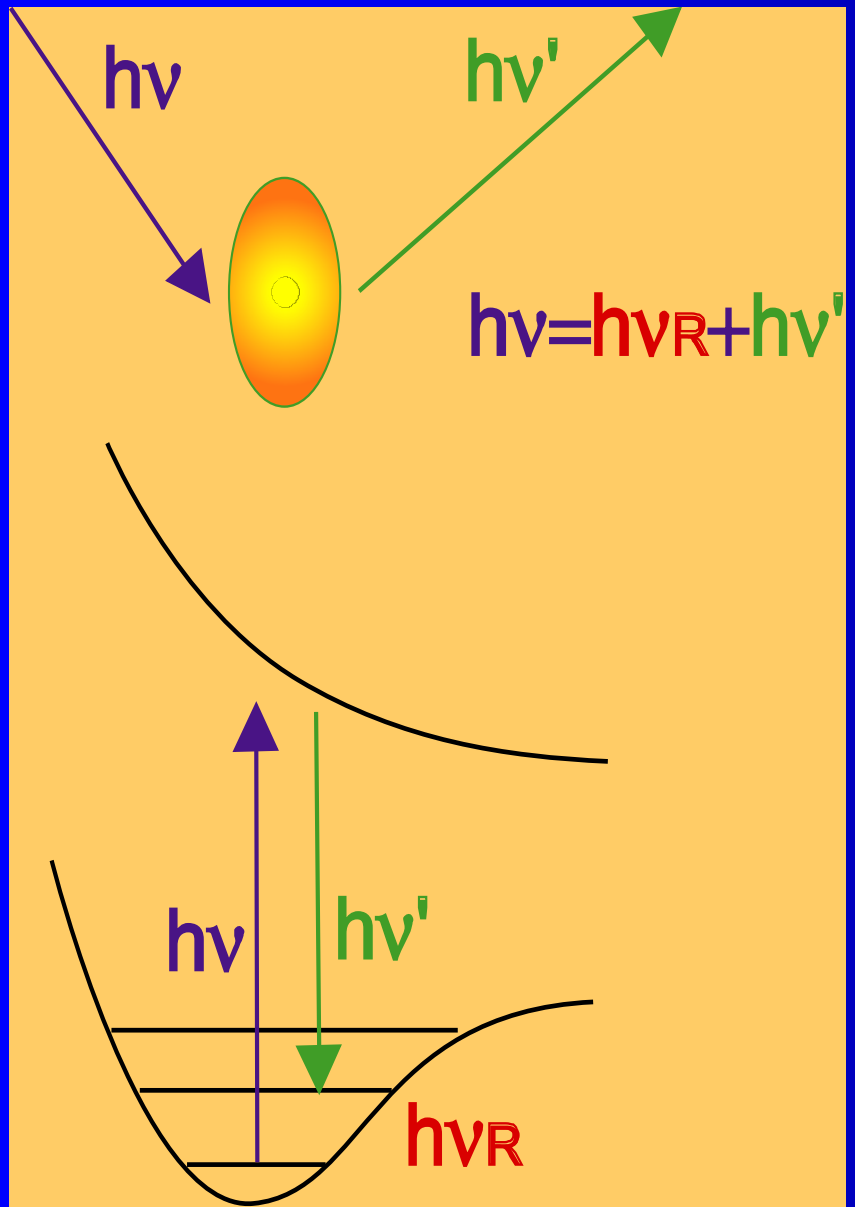




Molecule

Small cross section

Raman Scattering



Advantage:

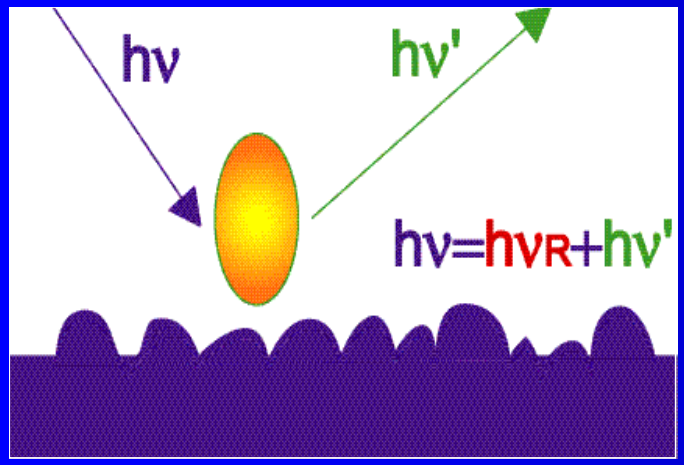
Molecule specific

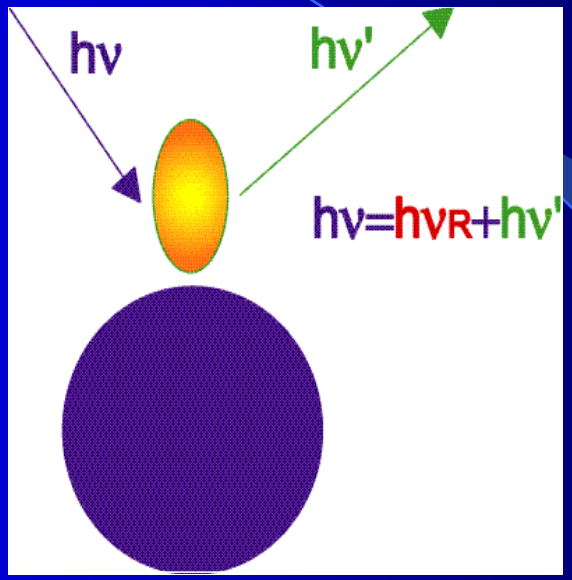
Disadvantage:

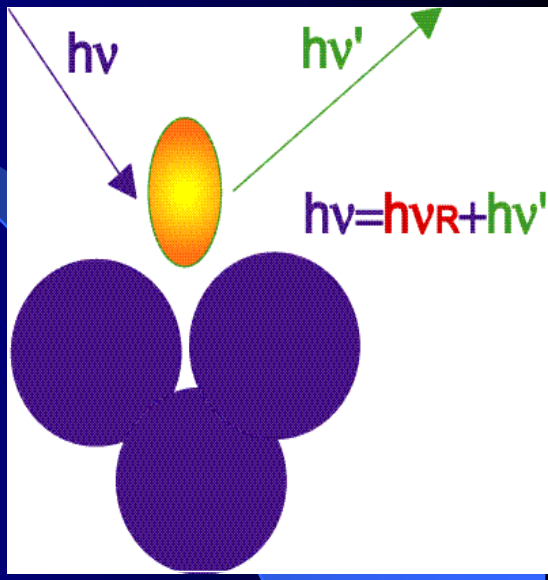
very small signal

(QY=10^{-6}-10^{-8})

SERS (Surface Enhanced Raman Scattering)





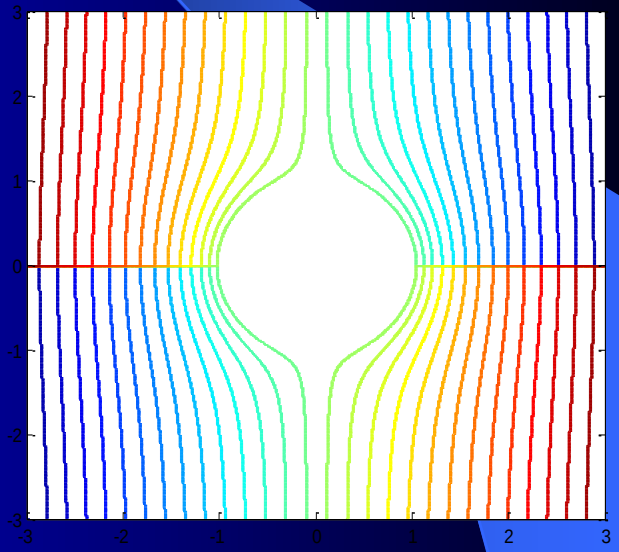


Roughened metal surface:
Enhancement=10^{6-8}

Metal nanoparticles or aggregates:
Enhancement=10^{8-15}

Nie, Emory, Science, 275, 1102, 1997;
Kneipp, et al. PRL, 78, 1667, 1997

Electromagnetic Field Enhancement Near Sharp Edges and Small Particles



Contour plot of the potential around a metal sphere

Mechanism of SERS

- Local Field Enhancement

  Enhancement of the local excitation field

  Enhancement of the local Raman scattering field

$$Psers(\nu_s) = N \bullet I(\nu_l)\left|A(\nu_l)\right|^2\left|A(\nu_s)\right|^2\sigma_{ads}^2$$

- Increase of the Raman scattering cross section

  Electronic coupling between molecule and metal (chemical effect)

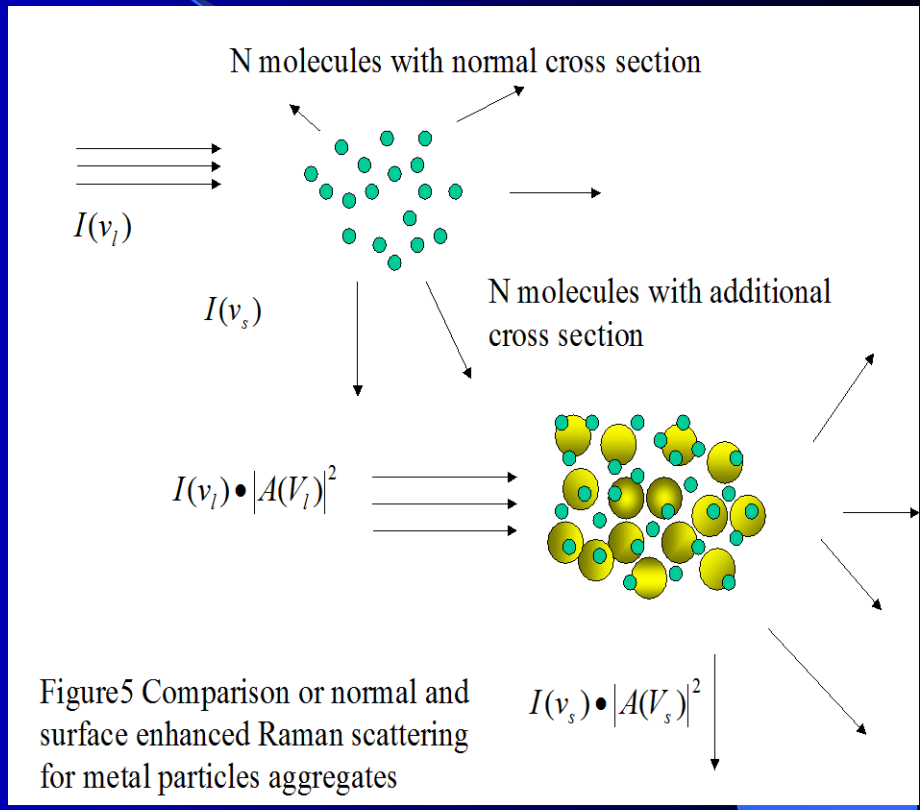


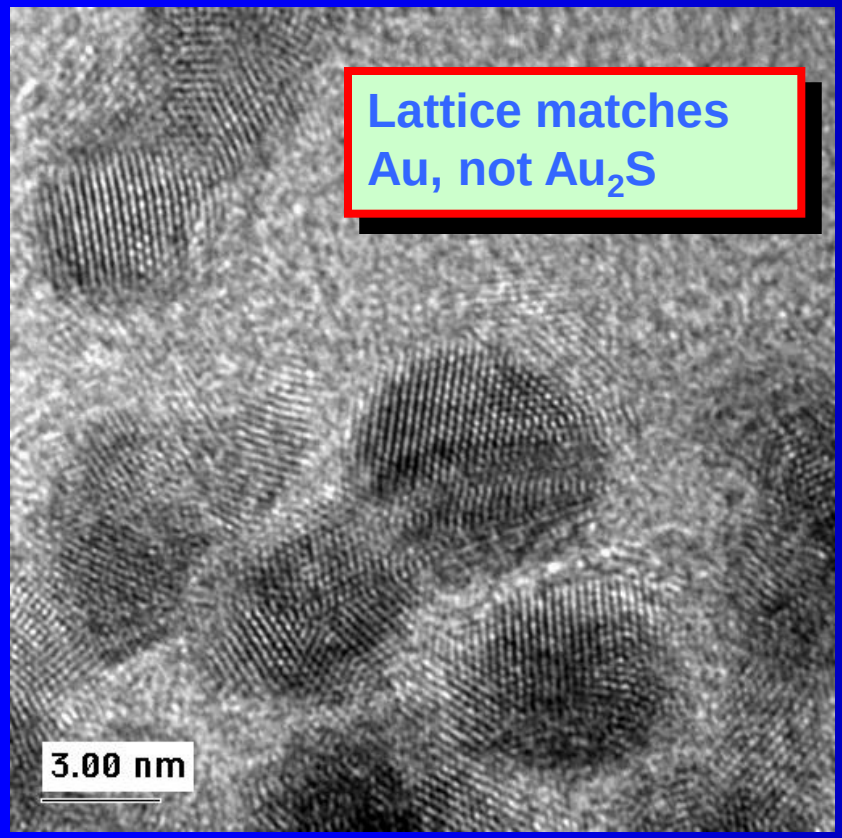
Figure5 Comparison or normal and surface enhanced Raman scattering for metal particles aggregates

Katrin Kneipp,et. al. Chem. Rev 99, 2957(1999)

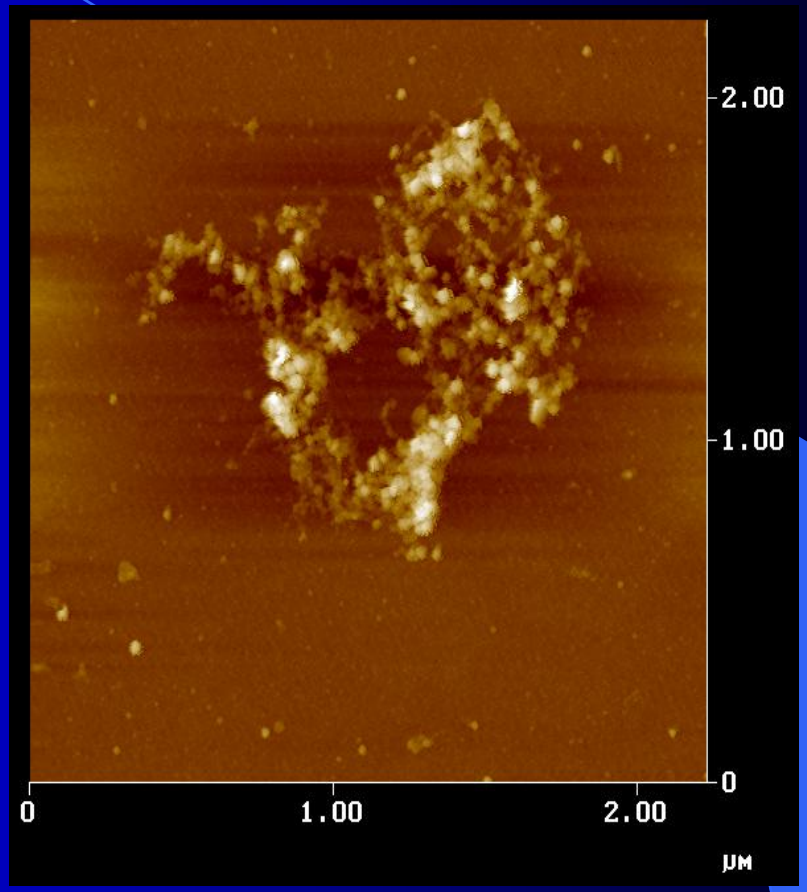
Two Critical Requirements for SERS

- Metal substrate must have resonance absorption of incident light (*absorption depending on size and shape of nanostructures*)
- Target analyte molecules must be very close to surface of metal substrate (*interaction depending on surface properties of substrate*)

HRTEM and AFM of Au Particles

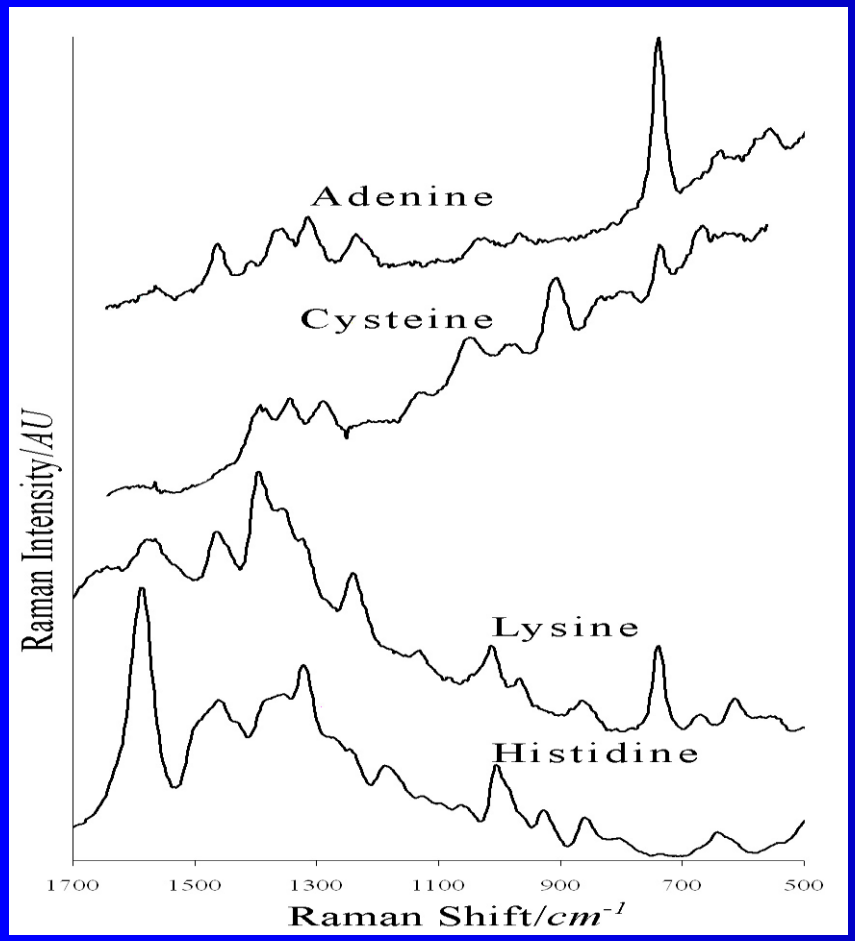


Lattice matches Au, not Au_2S

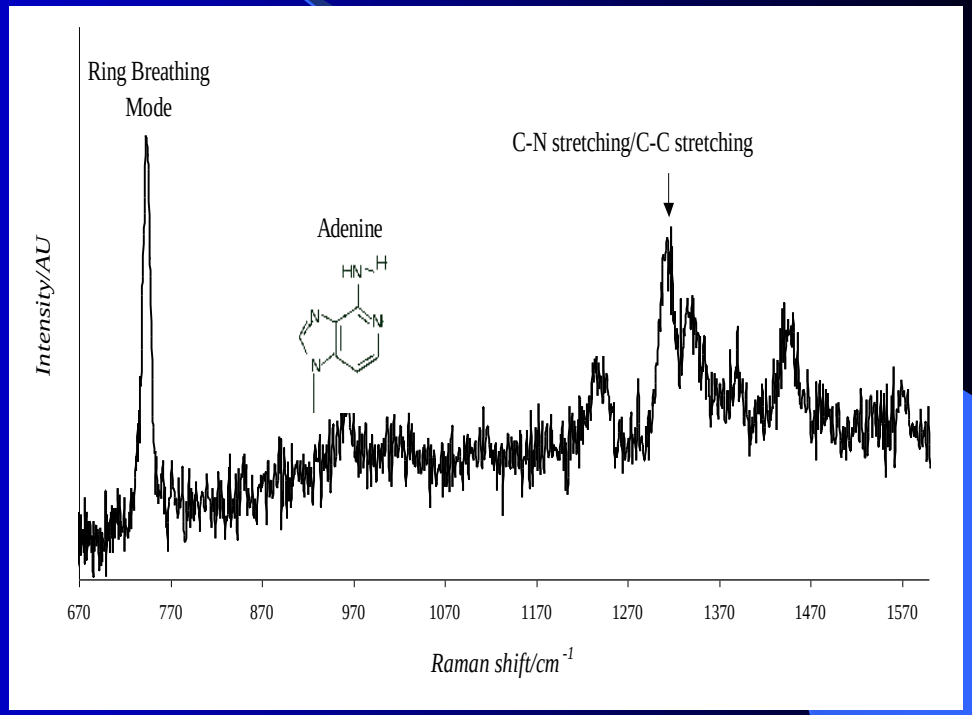


Evidence of Au aggregate

SERS Spectra of DNA Base and Amino Acids on Au NP Aggregates

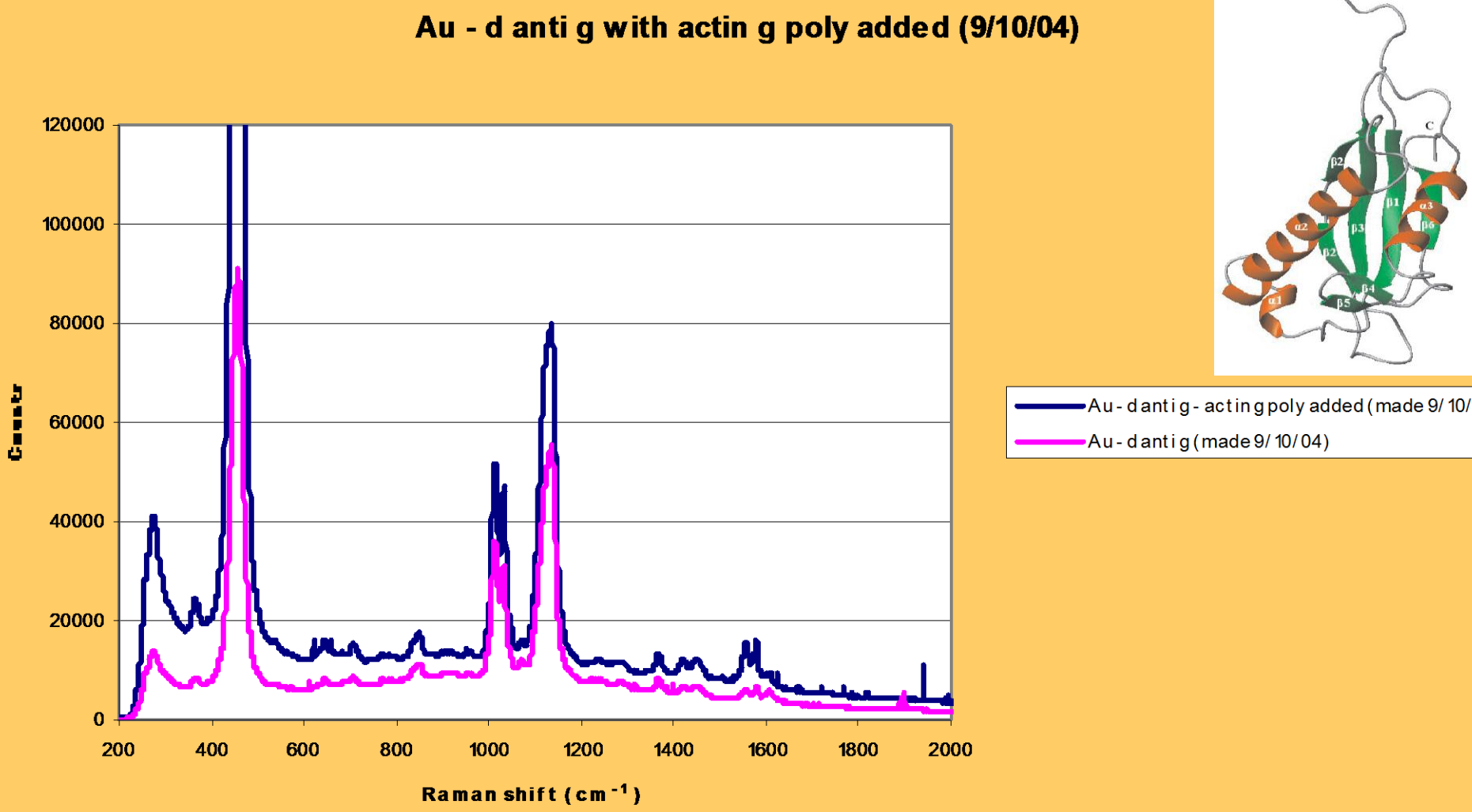


SERS of Adenine on a single aggregate

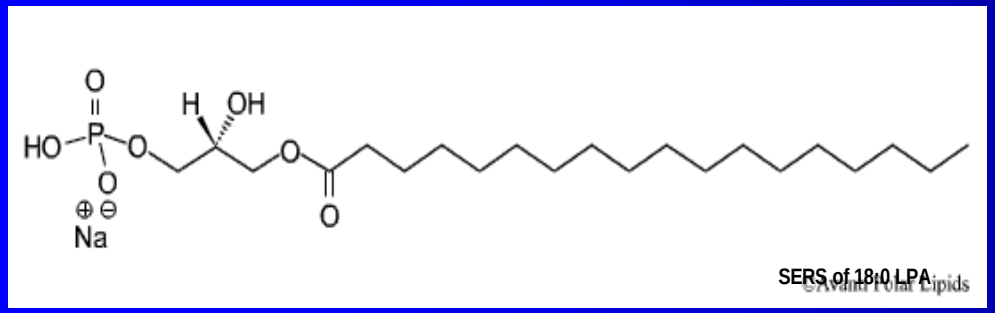


Schwartzberg, et al., JPCB, 108,19191, 2004

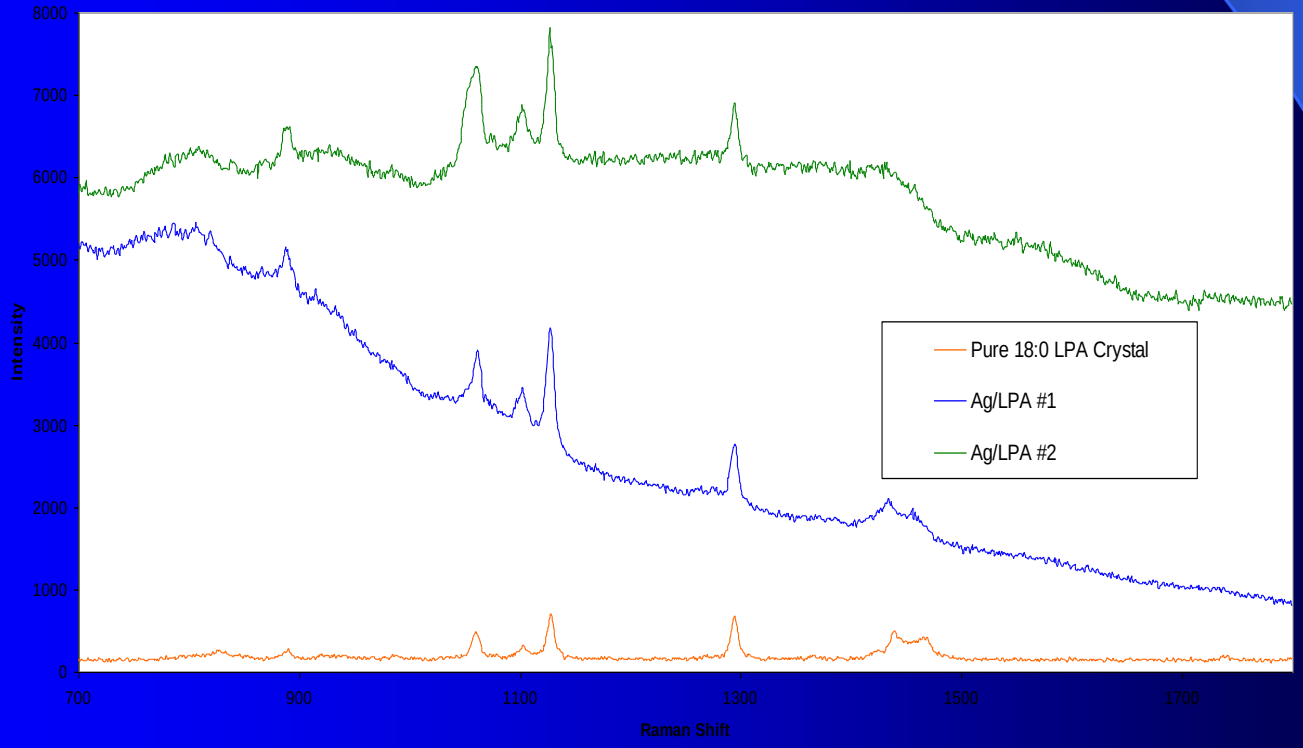
SERS of Polyclonal Antibodies: Donkey Anti-Goat IgG



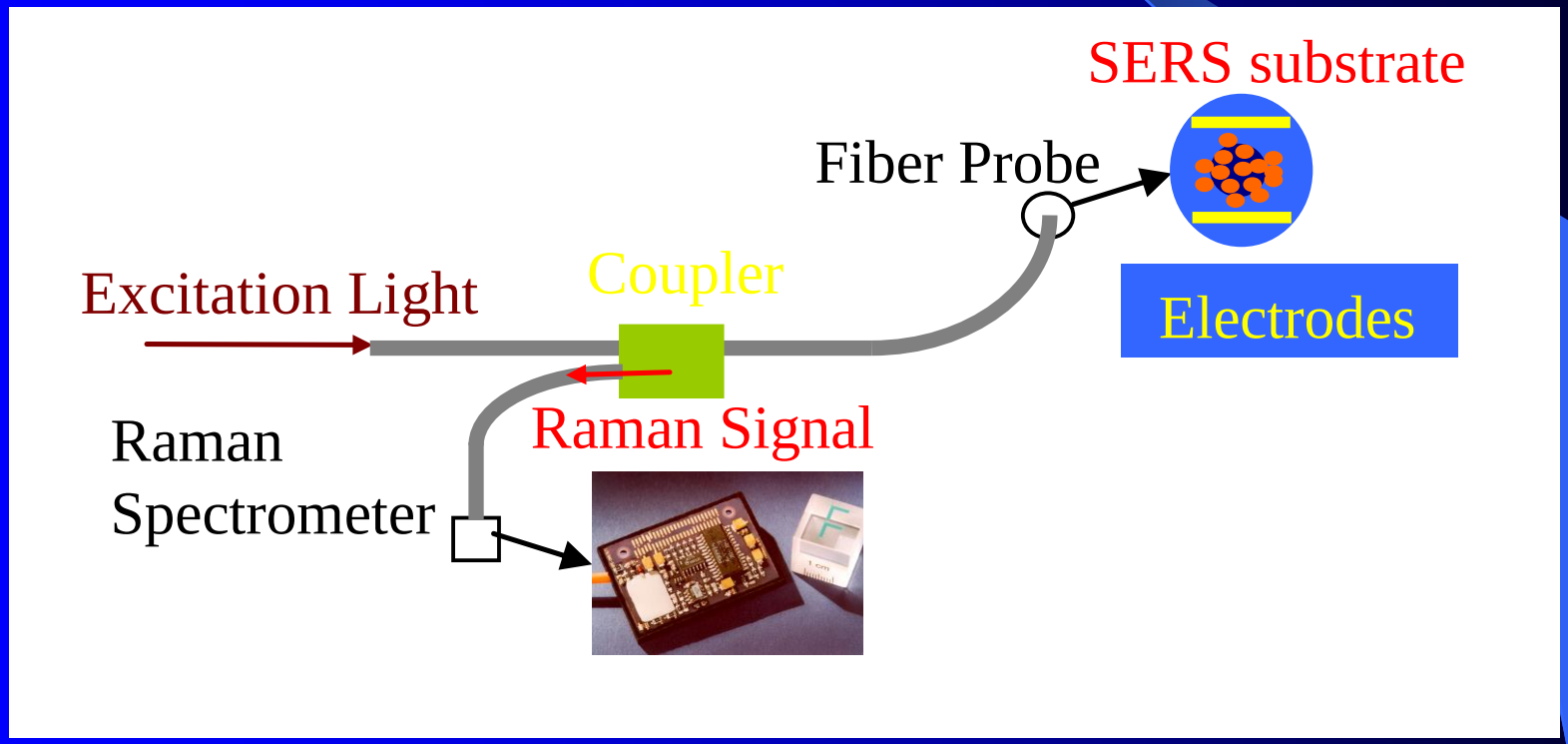
SERS Detection of an Ovarian Cancer Biomarker: LPA



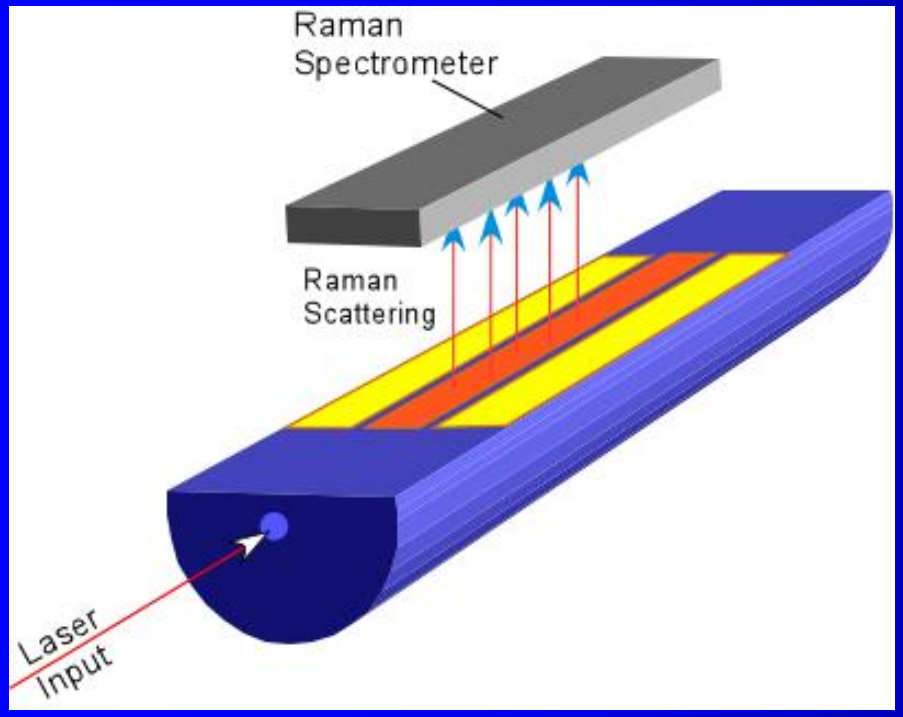
LPA: A unique ovarian cancer marker

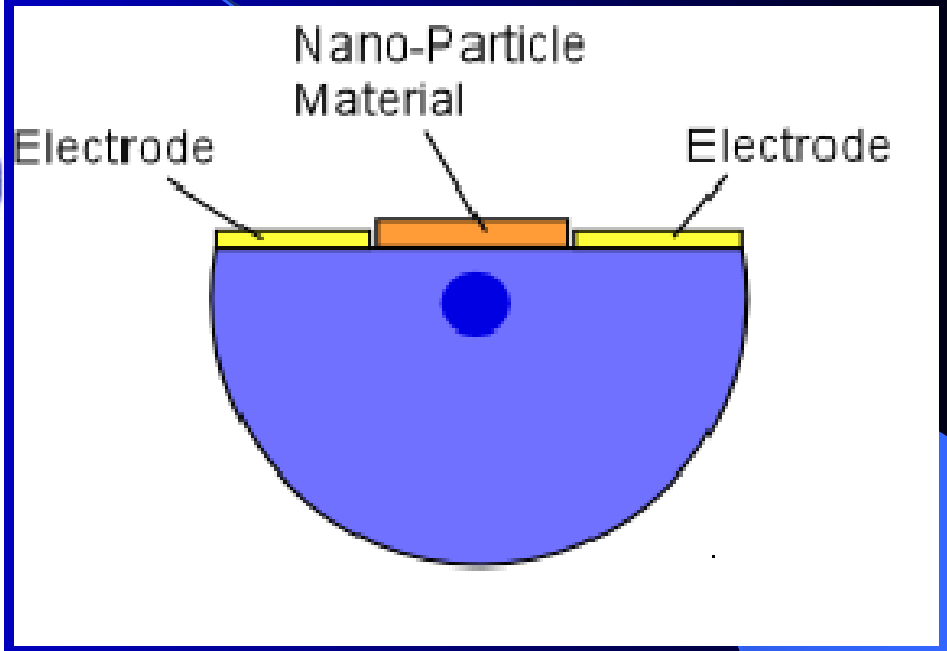


Ultra-sensitive Compact Fiber Sensor Based on Nanoparticle Surface Enhanced Raman Scattering



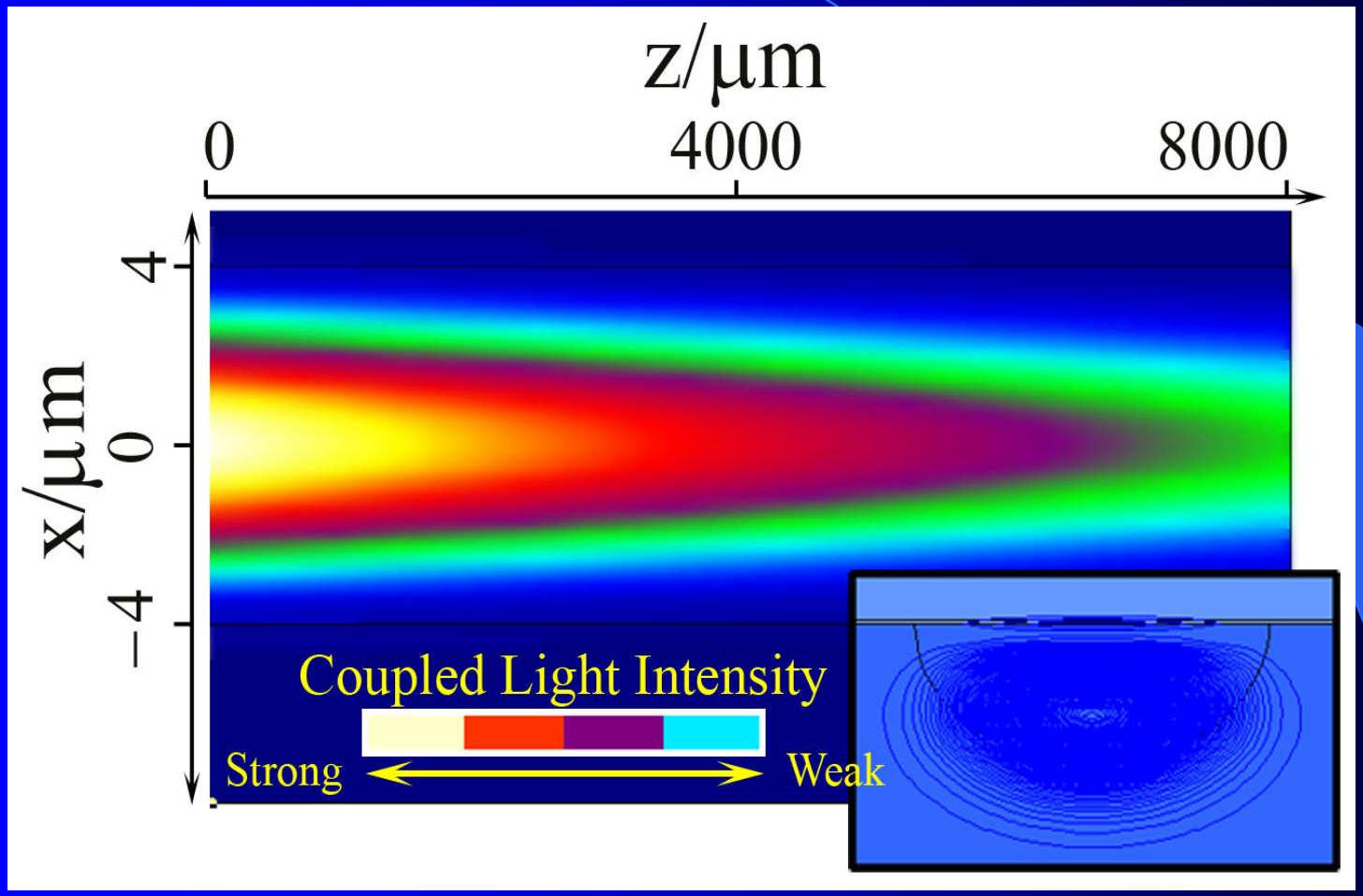
A Compact Platform for D-Shaped Fiber-Based SERS/Raman Sensor and Molecular Imaging Device



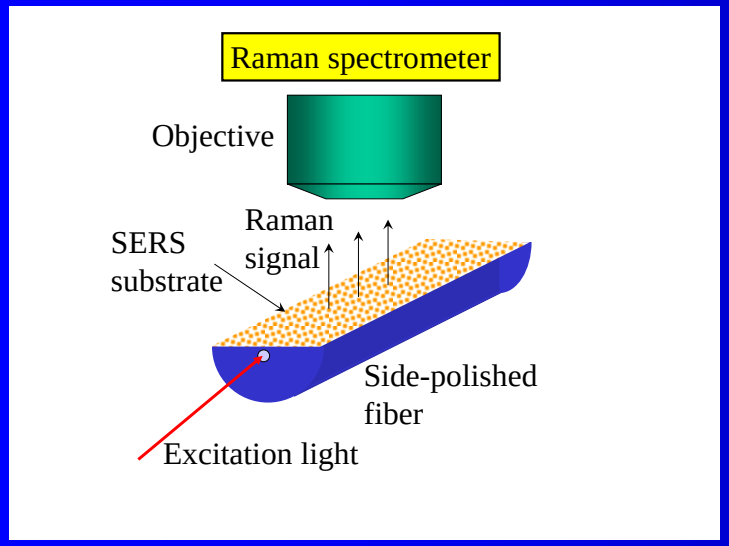


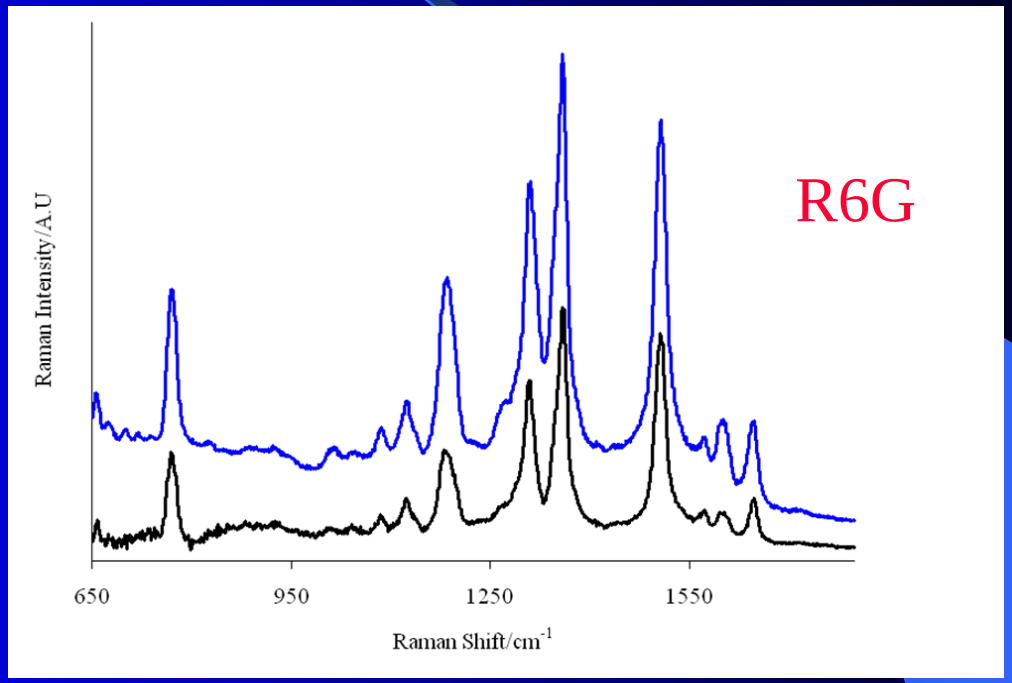
Non-invasive optical technique with unique combination of molecular specificity and extremely high sensitivity

Light Propagation and Coupling Inside a Side-Polished Fiber Covered with a Metal Overlay



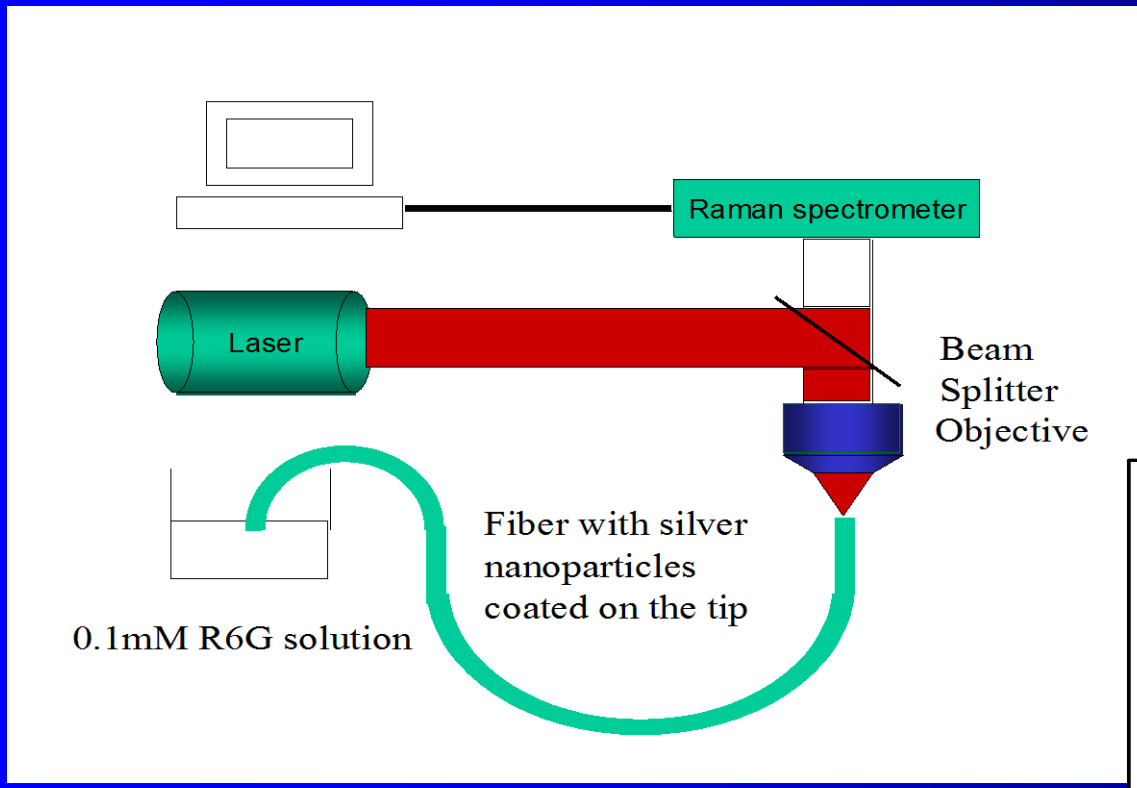
SERS Results for D-shaped Fibers with Side Detection

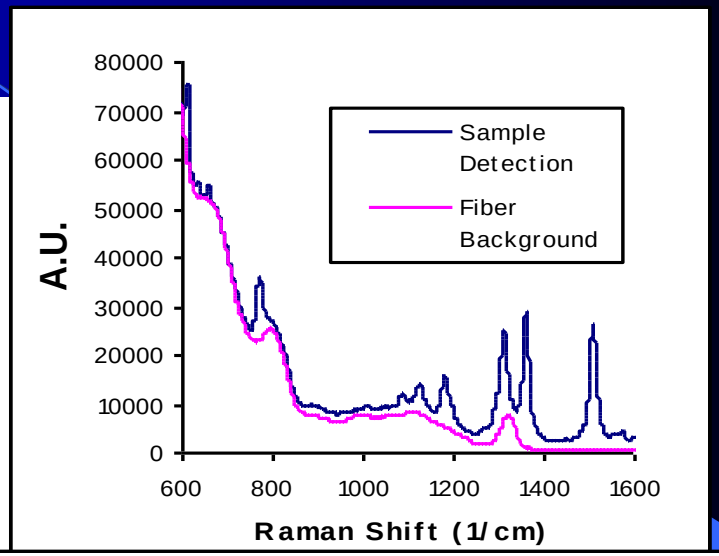


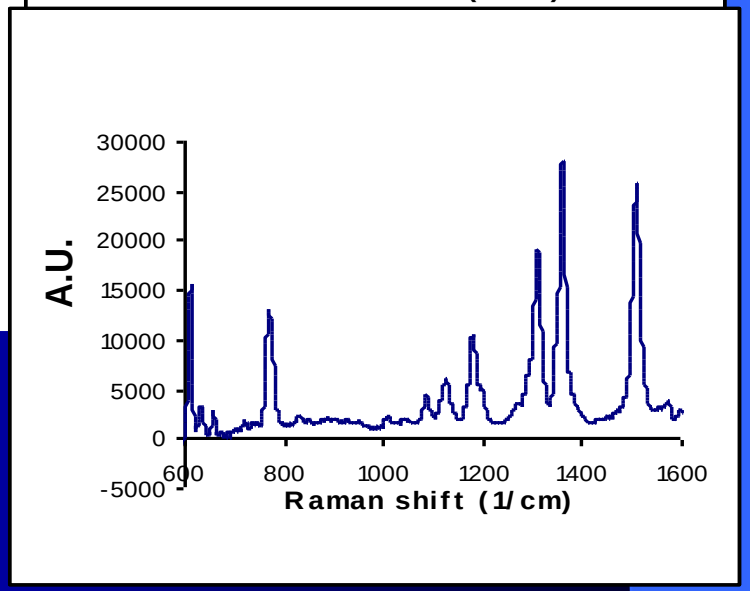


Zhang et al. Appl. Phys. Lett. 123105, (2005).

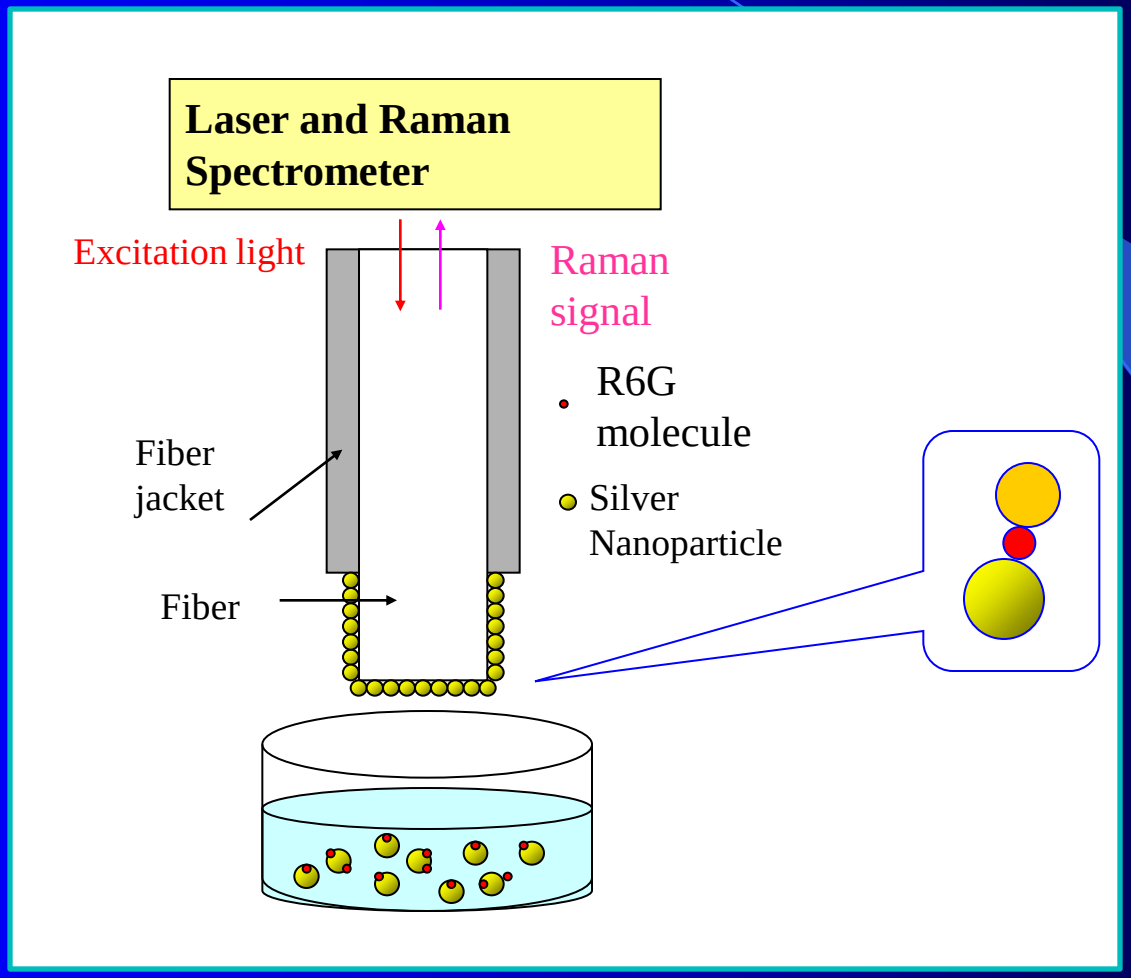
Tip Coated Multimode Fiber

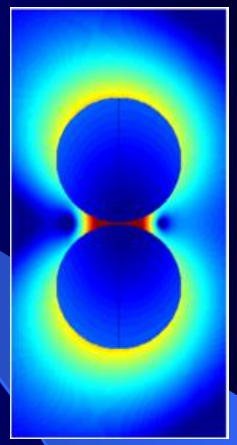






Double SERS Substrate "Sandwich" Fiber Probe — Tip-coated multimode fiber SERS probe

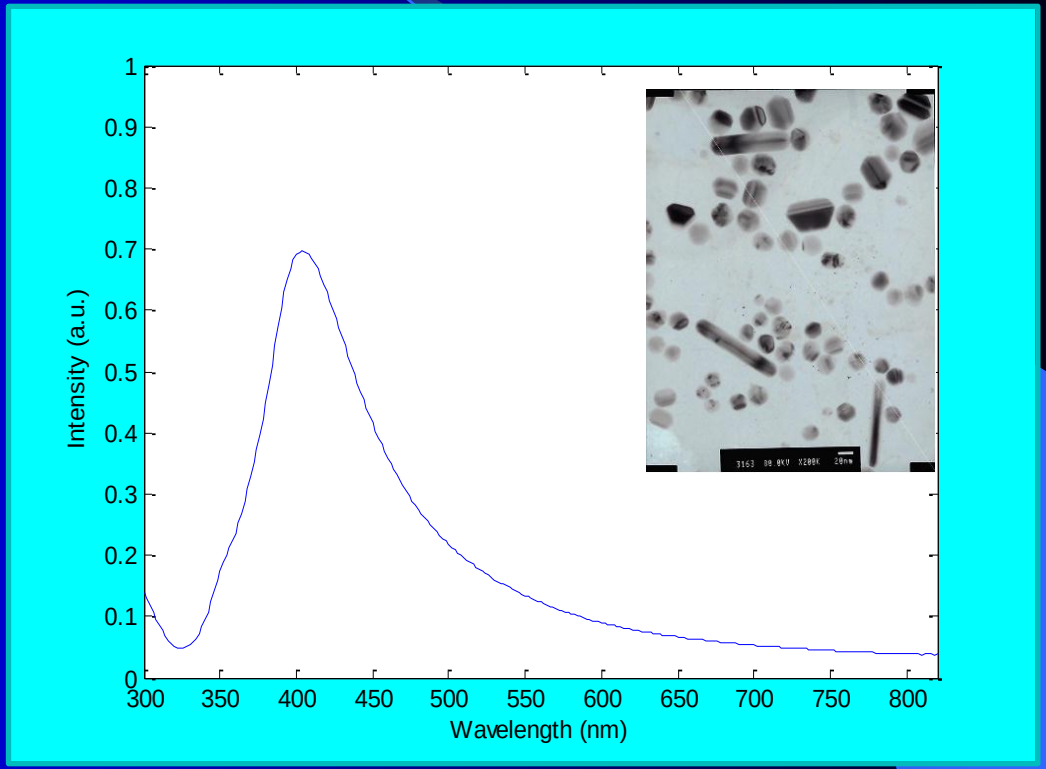




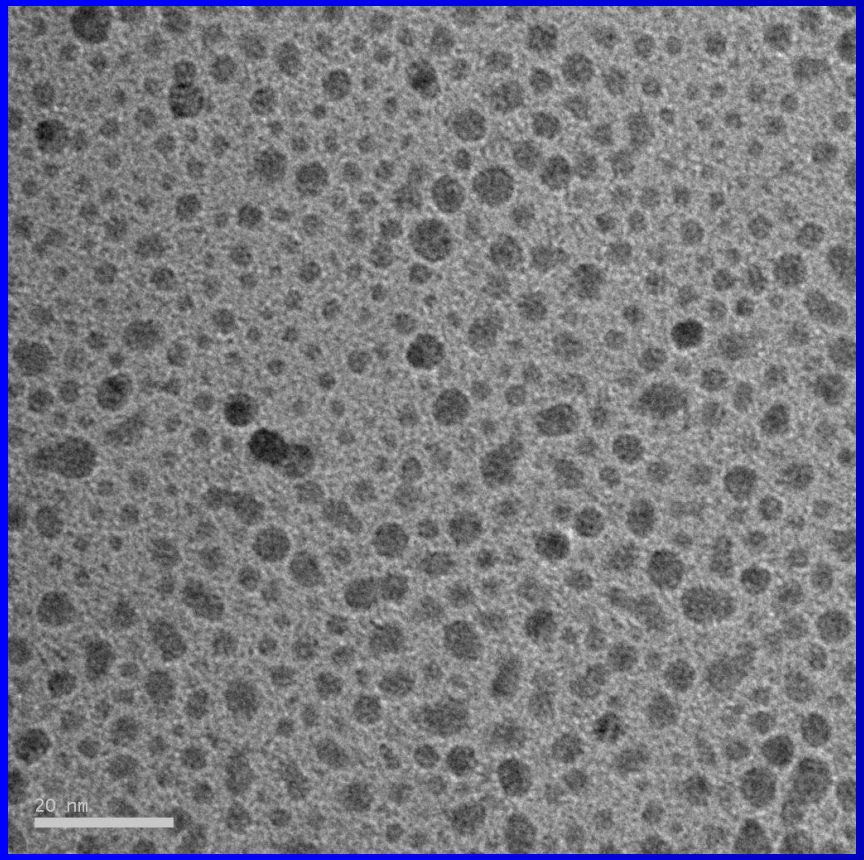
Chao Shi, He Yan, Claire Gu, Debraj Ghosh, Leo Seballos, Shaowei Chen and Jin Z. Zhang, *Appl. Phys. Lett.* **92,** 103107 (2008).

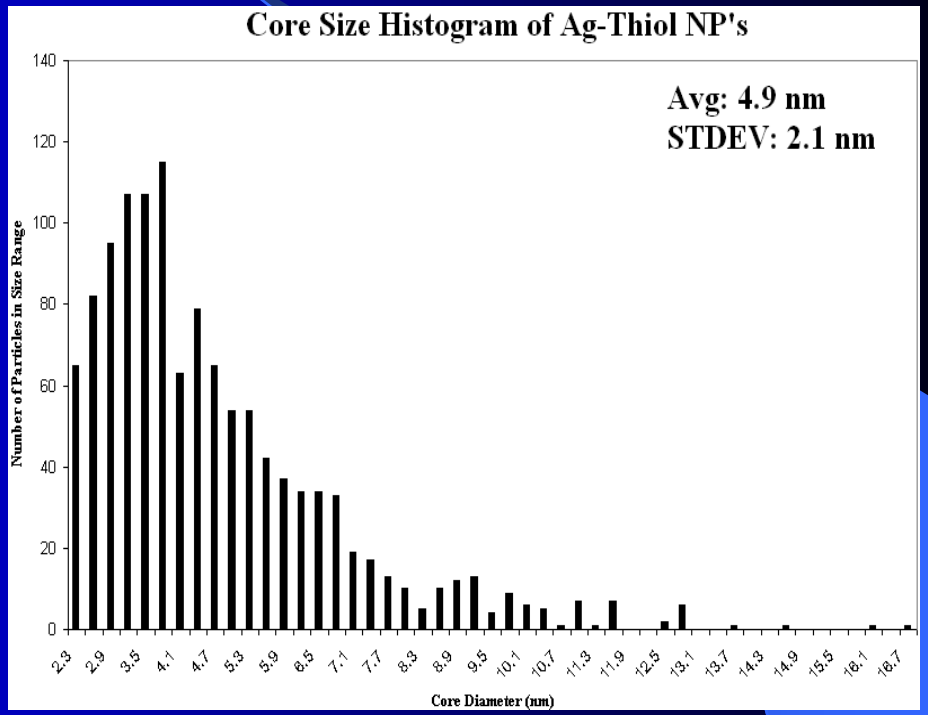
Synthesis of Silver nanoparticles (SNPs) in the sample solution

- Using a synthesis method from Lee and Meisel
- A concentration of 3.77×10^{-11} M
- Average diameter is 25 nm
- Solvent is water
- UV-vis absorbance curve exhibited a plasmon peak at 406 nm



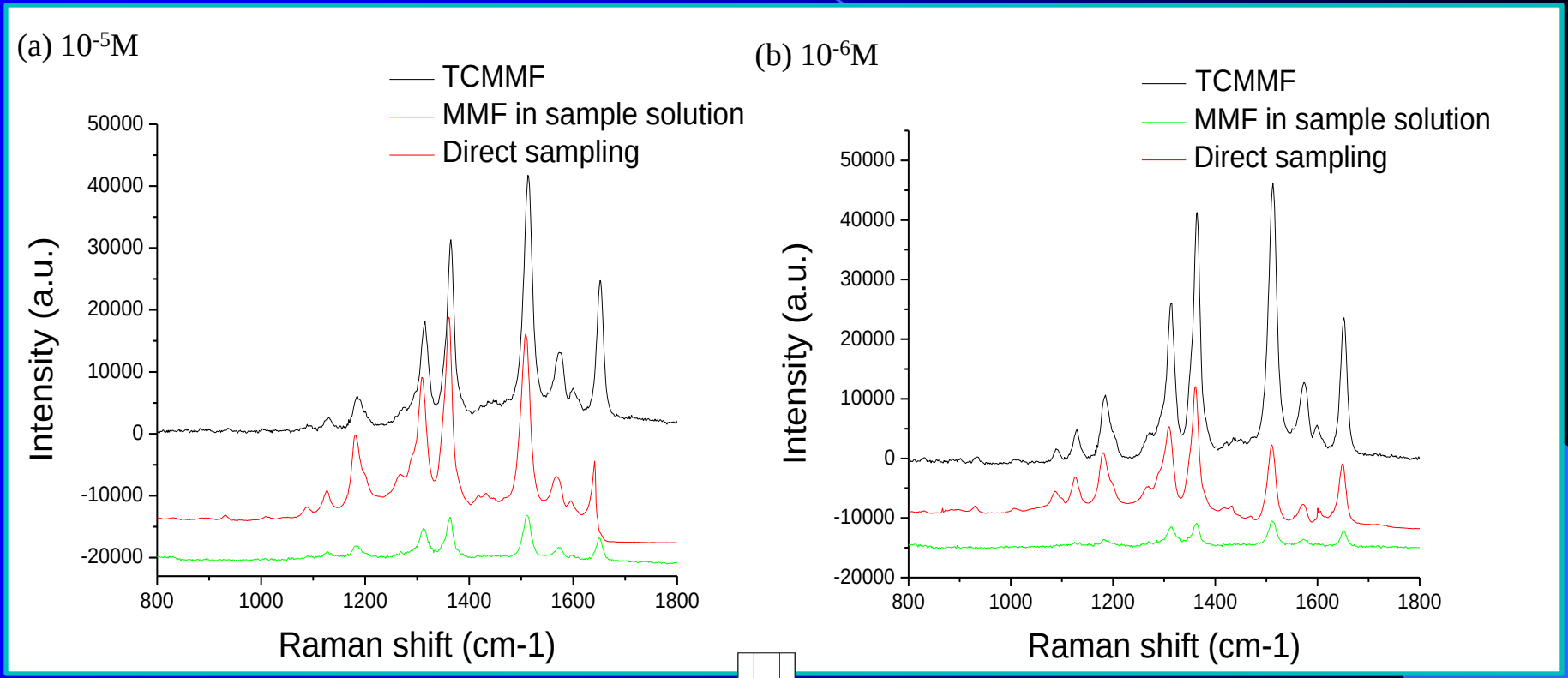
Silver nanoparticles on the tip

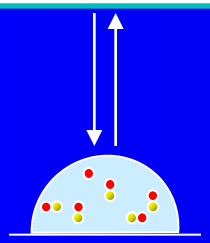




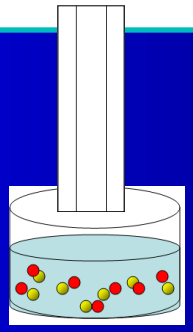
Using a synthesis method from modified Brust method and solvent is tetrahydrofuran (THF).

Results and Discussion





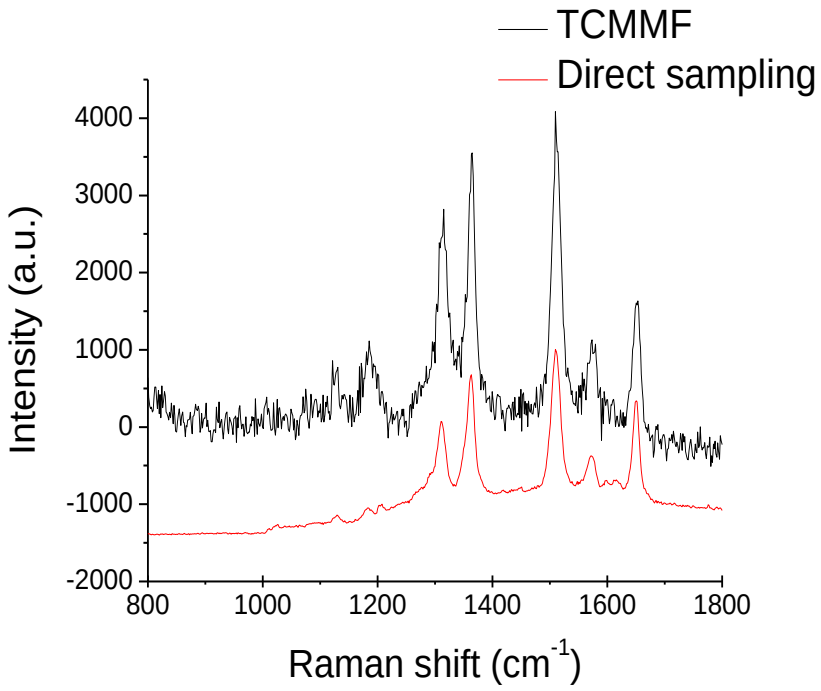
Direct sampling



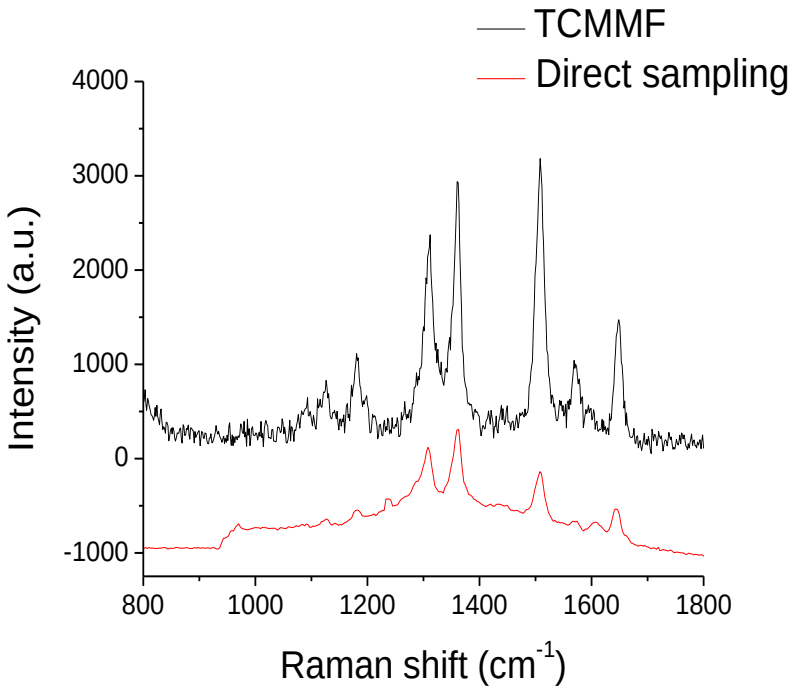
Uncoated MMF in sample solution

Results and Discussion

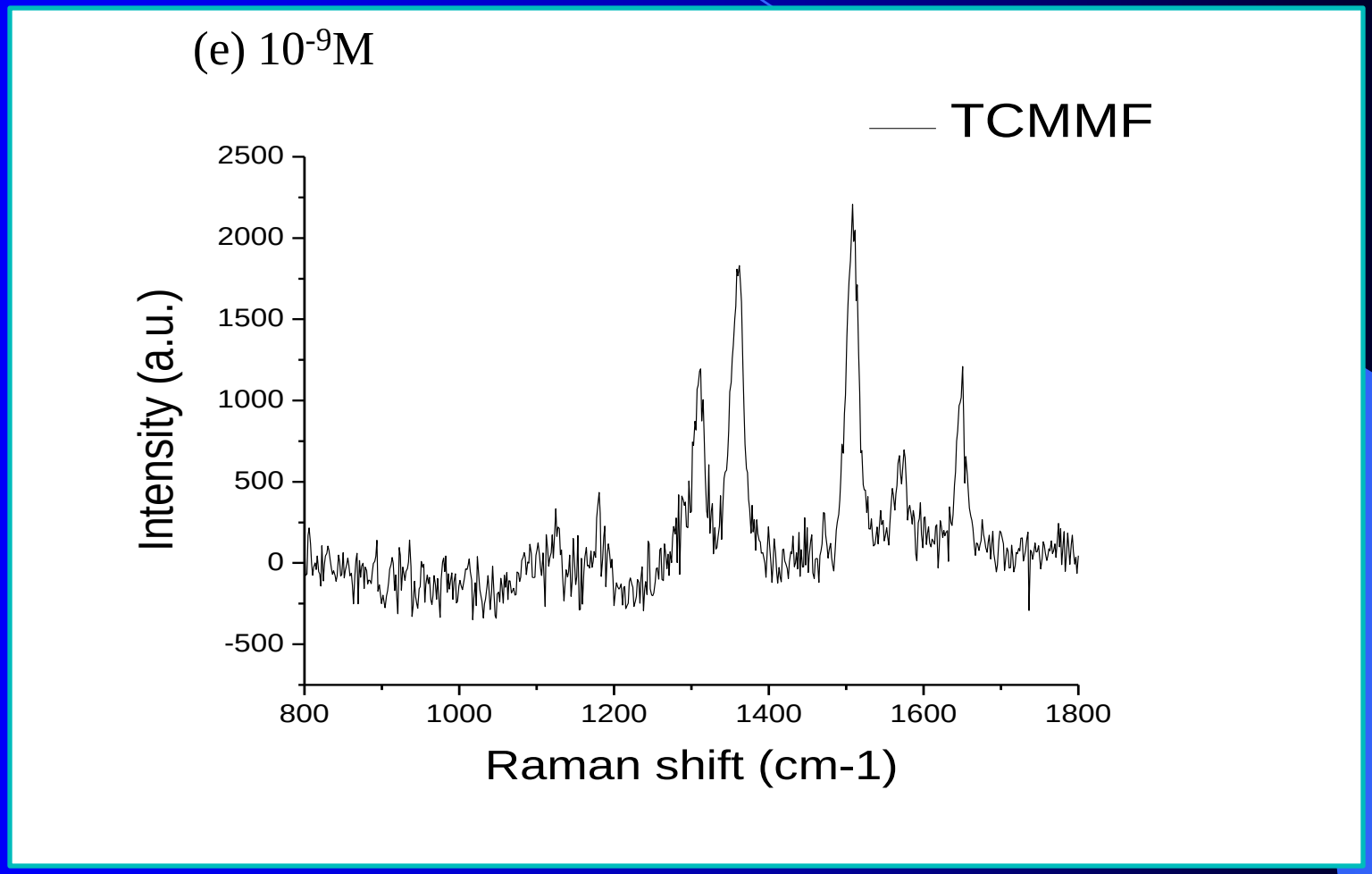
(c) 10^{-7}M



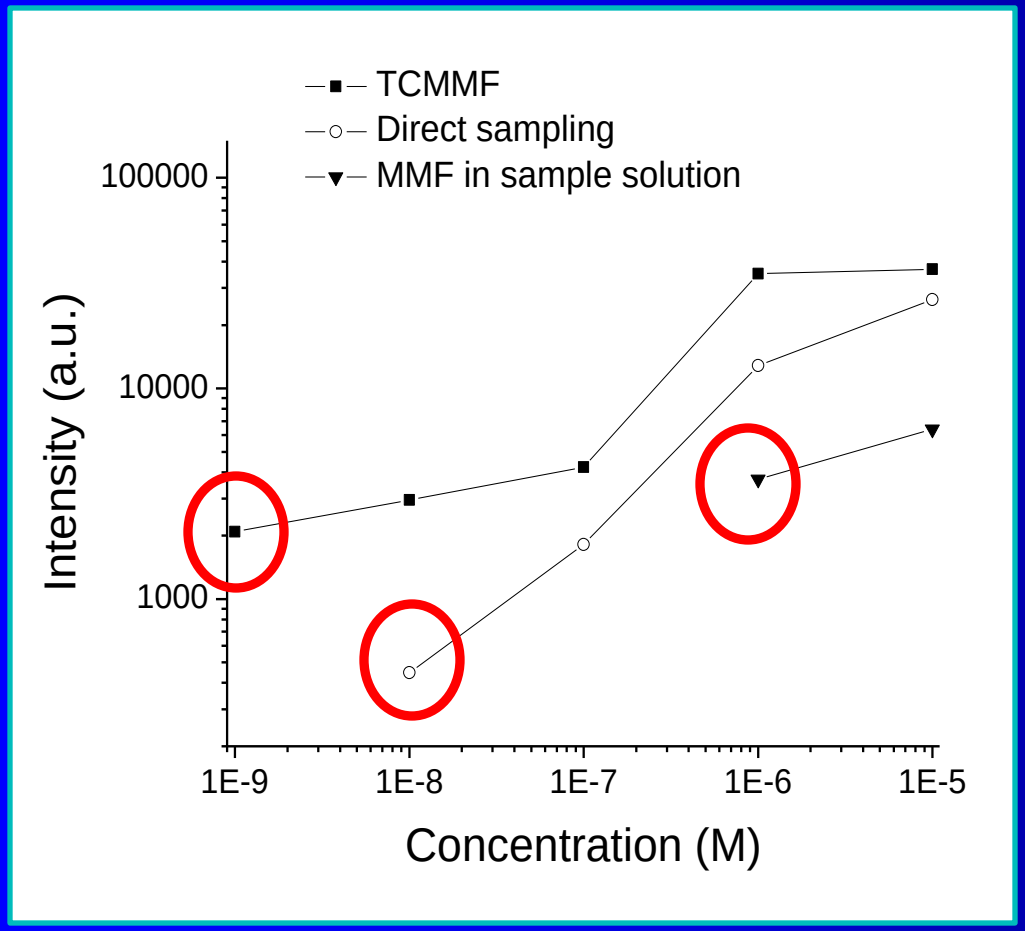
(d) 10^{-8}M



Results and Discussion



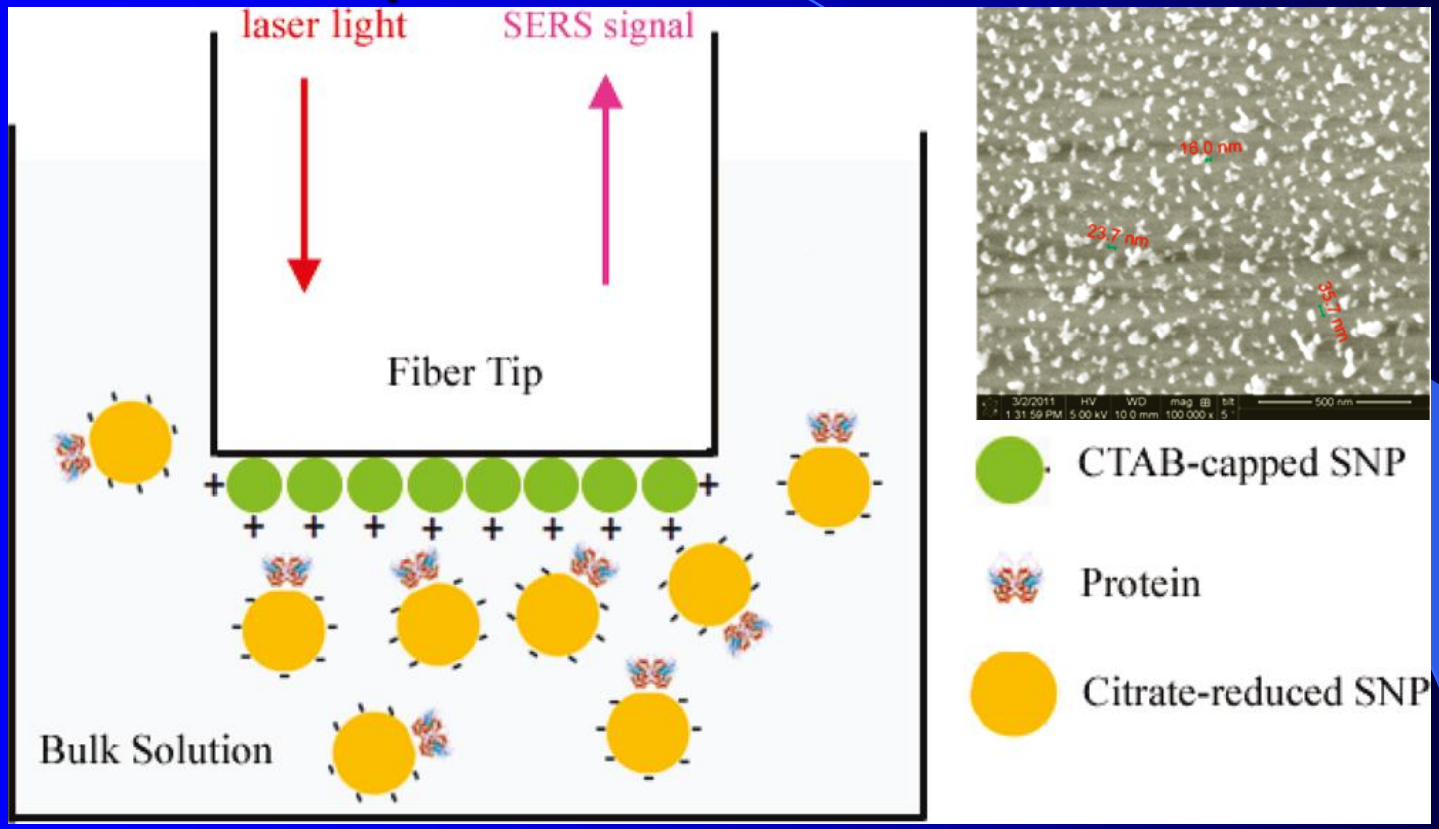
Comparison



Take peak 1514 cm^{-1} as an example.

1. The lowest detectable concentration for MMF, direct sampling and TCMMF are 10^{-6} M, 10^{-8} M, 10^{-9} M respectively.
2. TCMMF sensor has a higher sensitivity than other methods at the same concentration.
3. It demonstrated the stronger SERS activiety with the TCMMF due most likely to stronger EM field enhancement as a result of the unique sandwich structure.

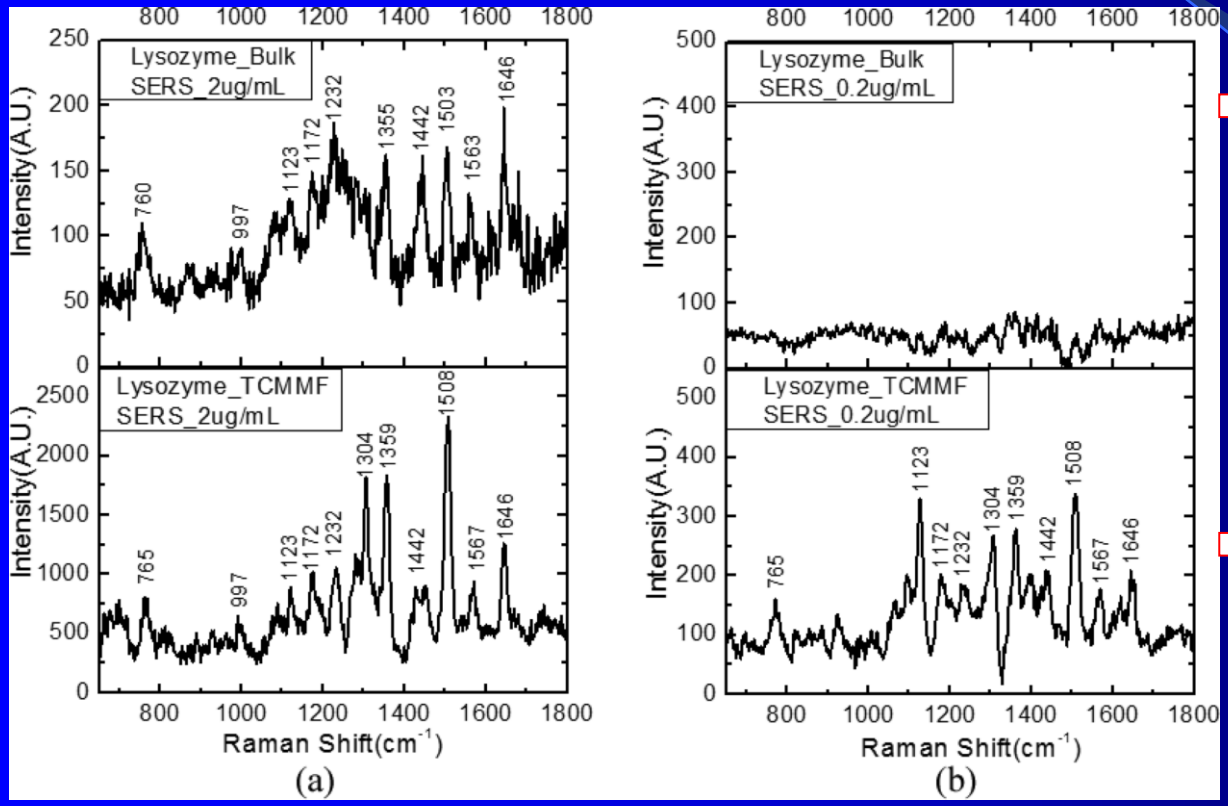
TCMMF with Oppositely Charged NPs for protein detection



- Oppositely charged double-substrate "sandwich" structure
- Larger silver nanoparticles (SNPs) coated on the fiber tip (25 nm vs. 5 nm)
- Easy and reproducible synthesis and coating

X. Yang, C. Gu, F. Qian, Y. Li, and J. Z. Zhang, Anal. Chem. **83**, 5888-5894 (2011).

TCMMF SERS probe operating in aqueous lysozyme detection

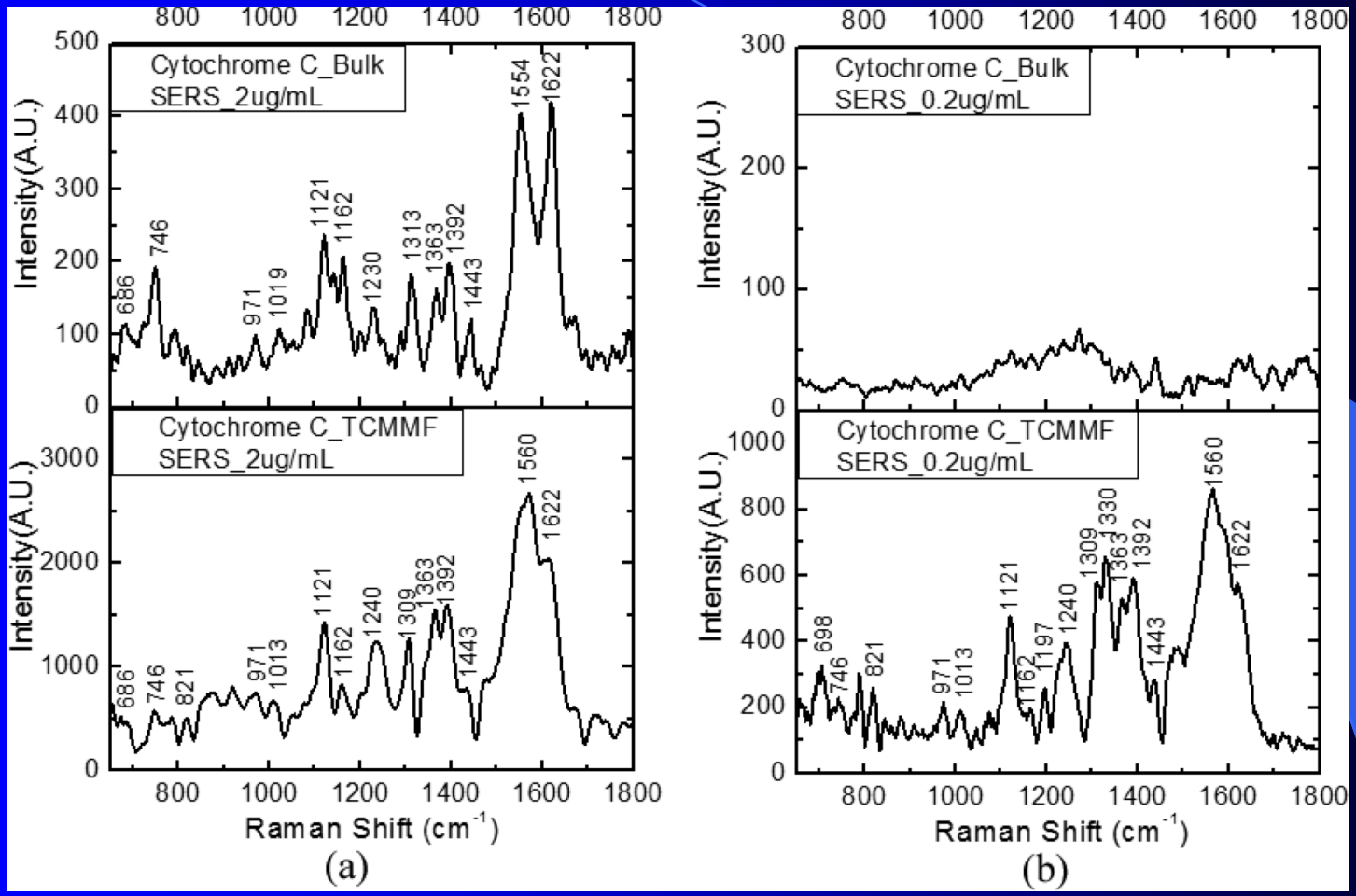


Similar to the detection limit in the literature* (5 µg/mL)

*X. Han et al., *Anal. Chem.* **81**, 3329-3333 (2009)

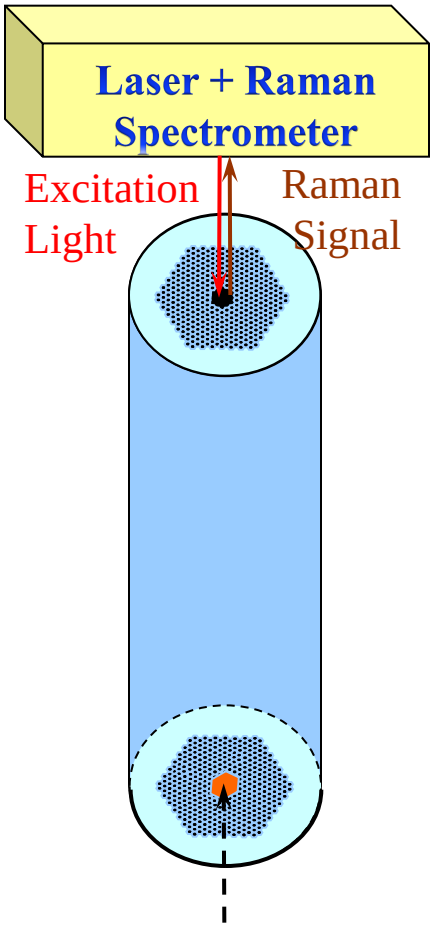
- One magnitude lower detection limit
- Average enhancement of 10 times but with variation for different peaks
- Advantages over dried-film strategy: higher reproducibility, flexibility and potentially in-situ remote sensing capability.
- Integration with a portable Raman spectrometer

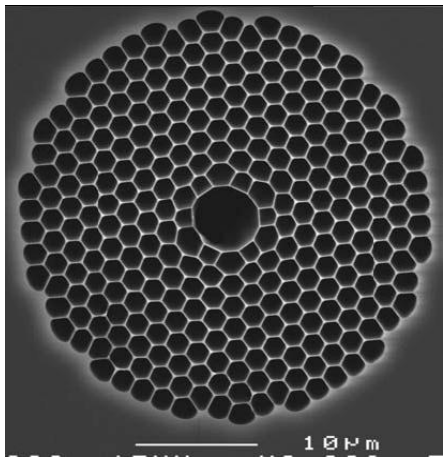
TCMMF SERS probe operating in aqueous cytochrome c detection



Some new peaks are observed at 821, 1197, and 1330 cm^{-1} and can be attributed to Tyr; Tyr and Phe; and Trp, respectively. In addition, the sensitivity enhancement varies for different peaks, with an average enhancement factor of 7

Liquid core photonic crystal fiber (LCPCF) Probe

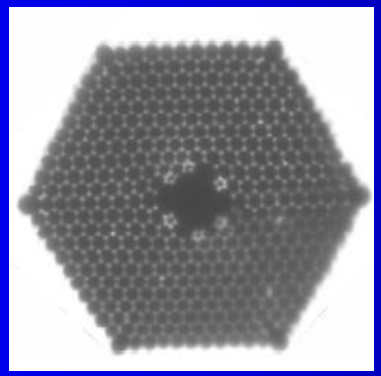


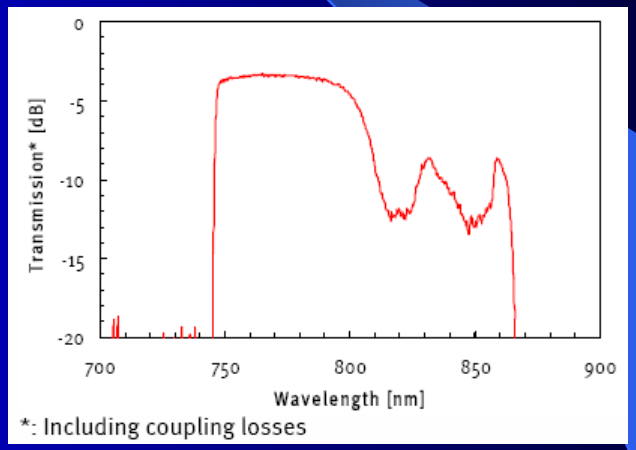


Yi Zhang, Chao Shi, Claire Gu, Leo Seballos and Jin Z. Zhang, *Appl. Phys. Lett.* **90**, 193504 (2007).

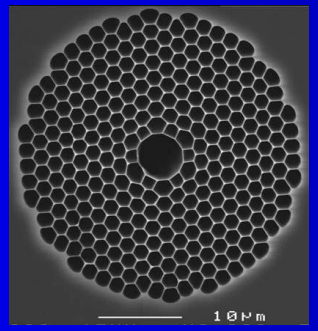
Photonic Crystal Fibers

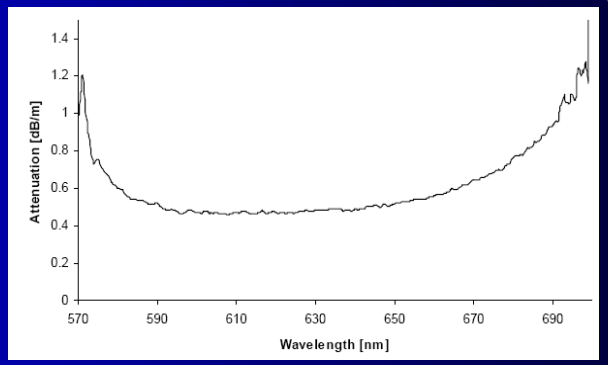
- Air-Guiding Hollow Core Photonic Bandgap Fiber:
  - AIR-6-800: 785nm





  - HC-633-01: 633nm





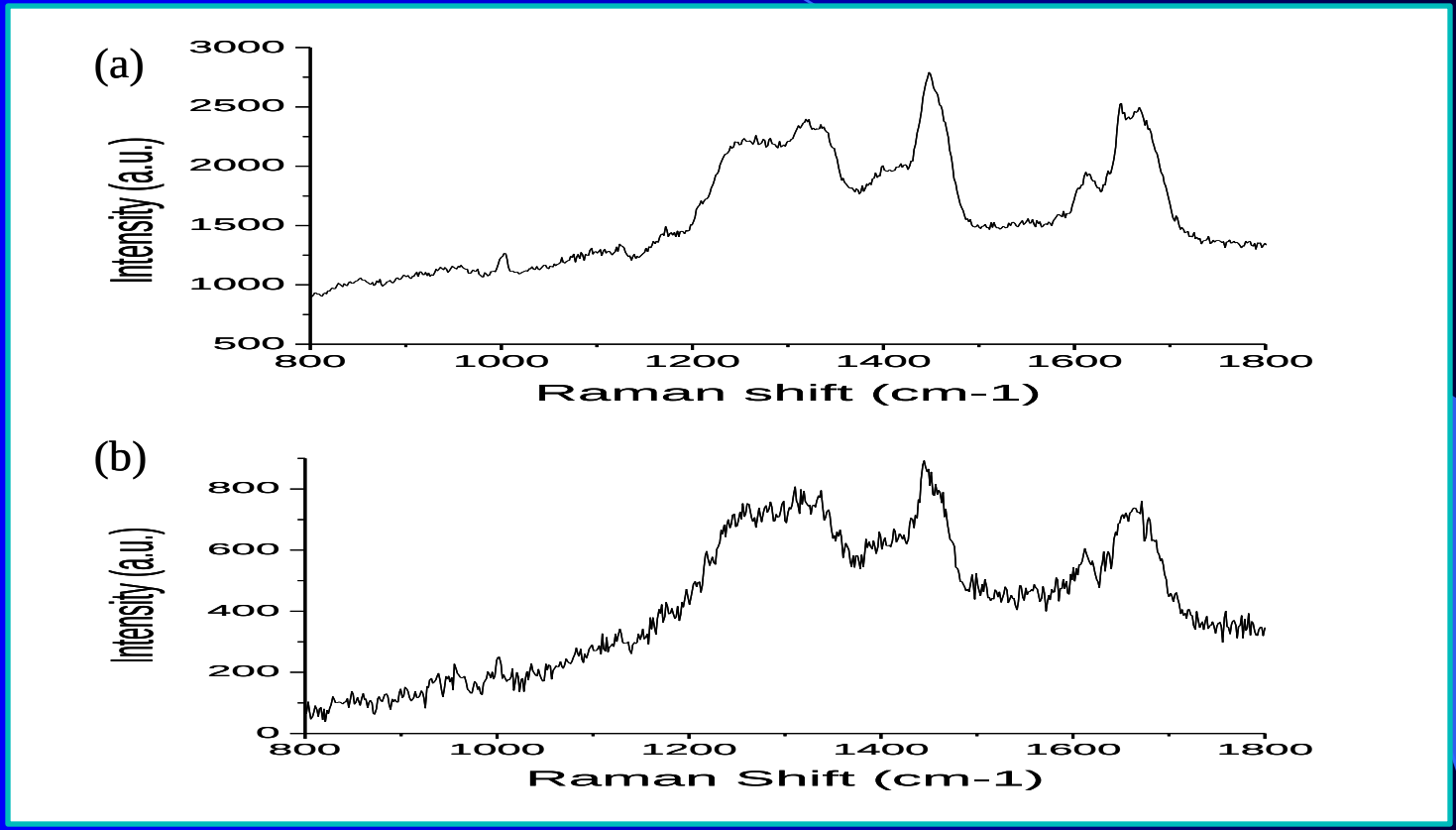
Prepare the PCF

- Cut the two end of the fiber carefully, keep the length about 10 cm.
- Seal the cladding holes of PCF by heat.

Torch

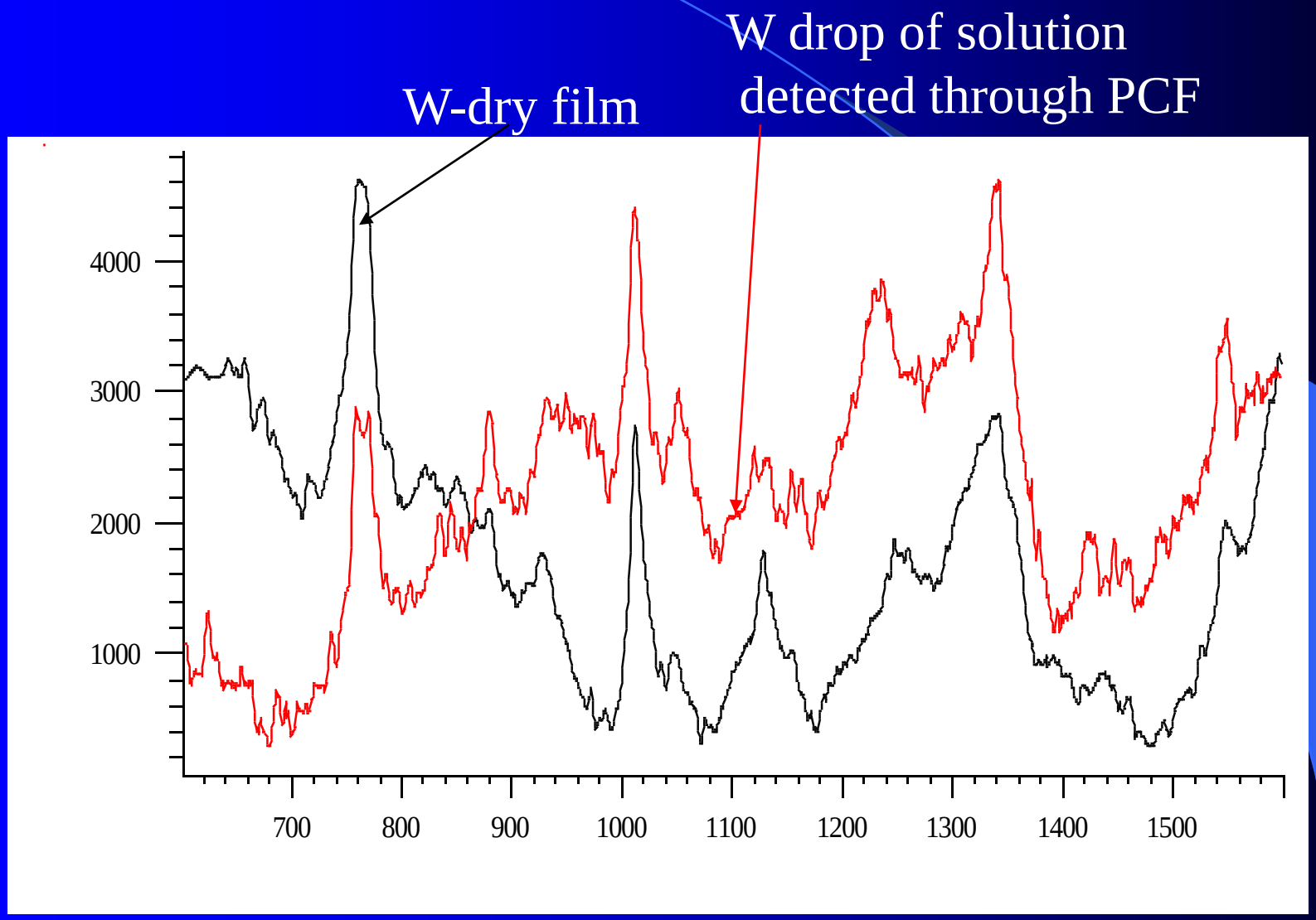
FITEL S175 fusion splicer

Alpha-synuclein detection using LCPCF sensors



- (a) (b) were collected with the 633 nm laser at 3 mW and a scanning period of 10 s.
- With the introduction of the silver binding peptides, the detectable concentration reached 10^{-4} M~ 10^{-5} M.

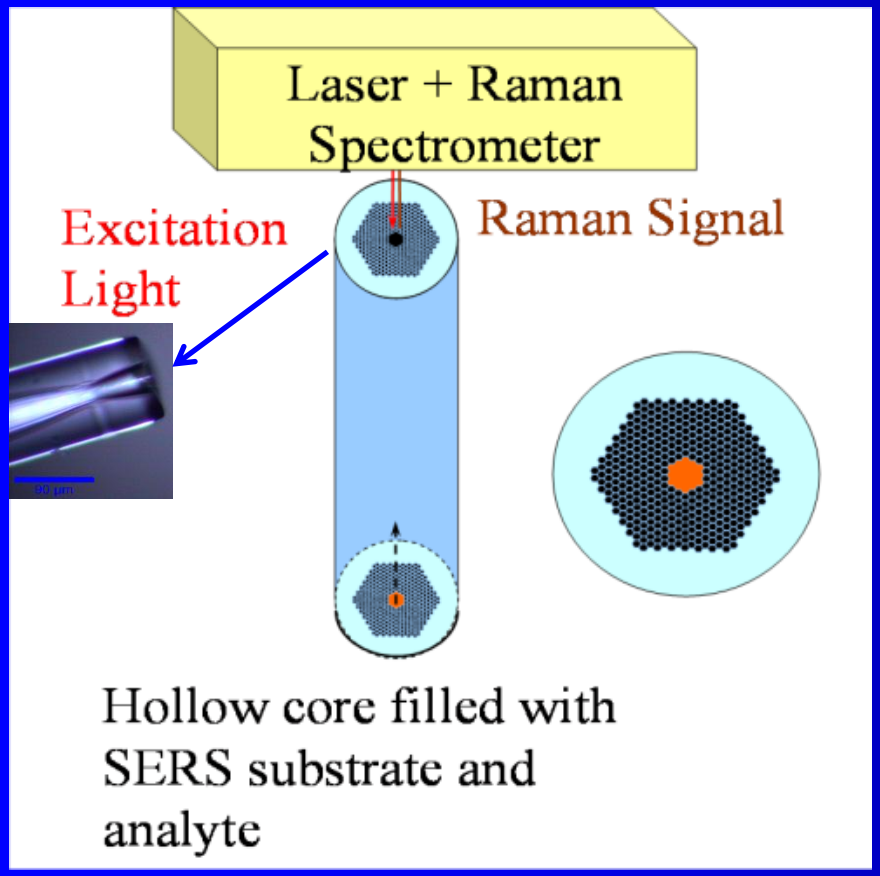
Tryptophan-W

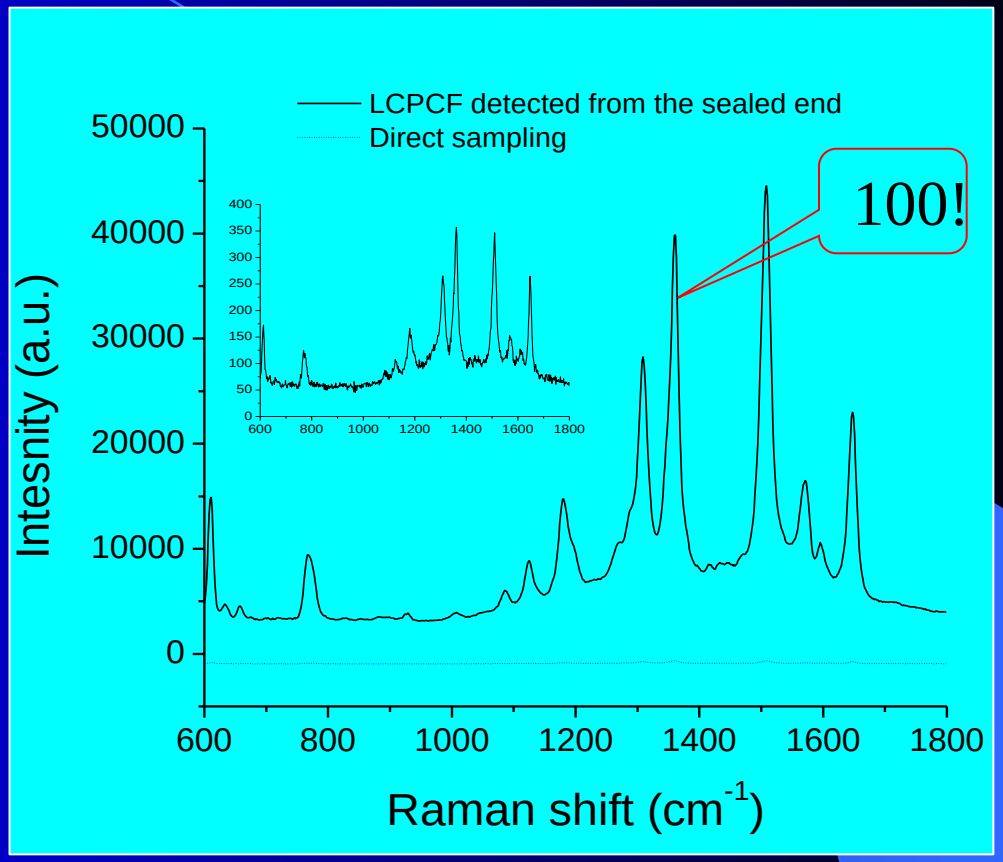


Same laser power

Additional Sensitivity Enhancement

Liquid core photonic crystal fiber SERS probe



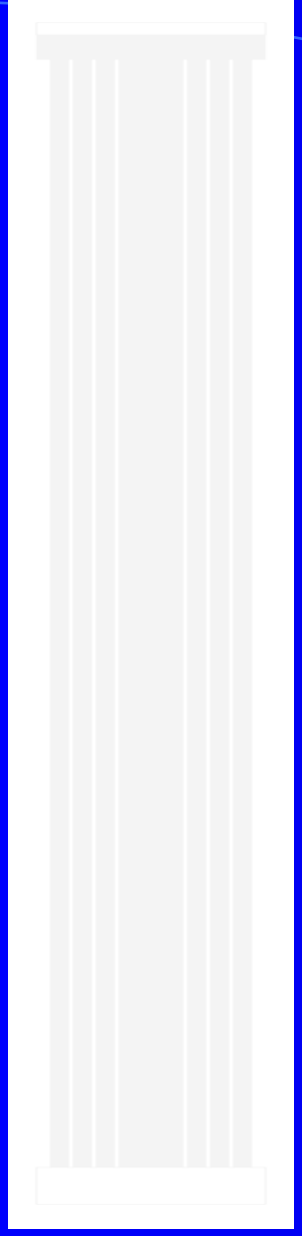


C. Shi, C. Lu, C. Gu, L. Tian, R. Newhouse, S. Chen, and J. Z. Zhang, *Appl. Phys. Letts.* **93**, 153101 (2008).

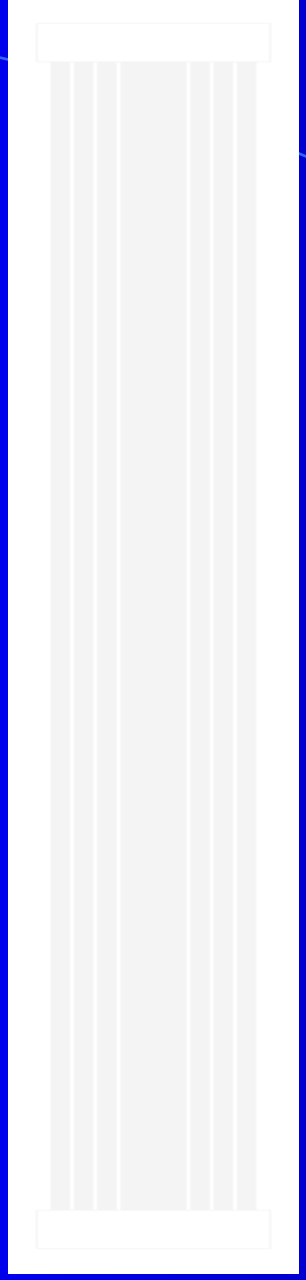
X. Yang, C. Shi, D. Wheeler, R. Newhouse, B. Chen, J. Z. Zhang and C. Gu, *J. Opt. Soc. Am. A*, **27**, 977 (2010).

FDTD Analysis

- Liquid core changes the index of refraction so that the Gaussian beam is almost confine in the core
- Strong EM field near the walls
- Nanoparticles prefer to attach to the walls
- And the larger interaction volume due to the confinement of light and sample
- Additional enhancement of SERS signal due to the PCF



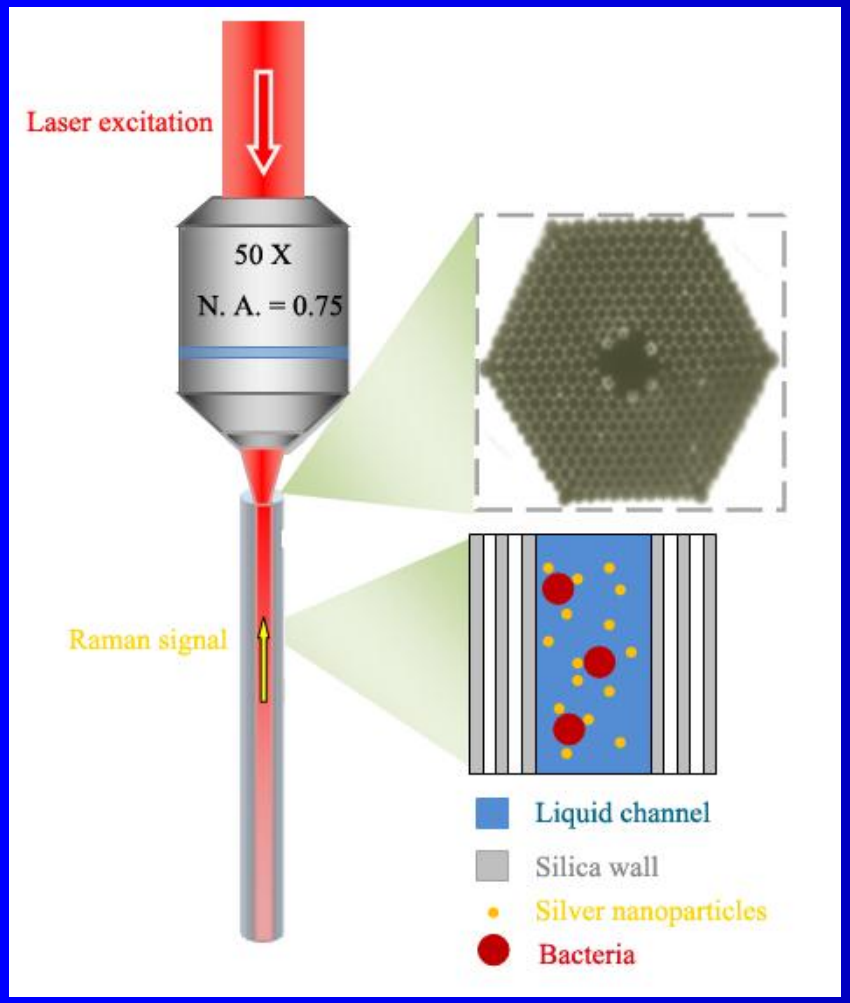
Transverse electrical field



Longitudinal electrical field

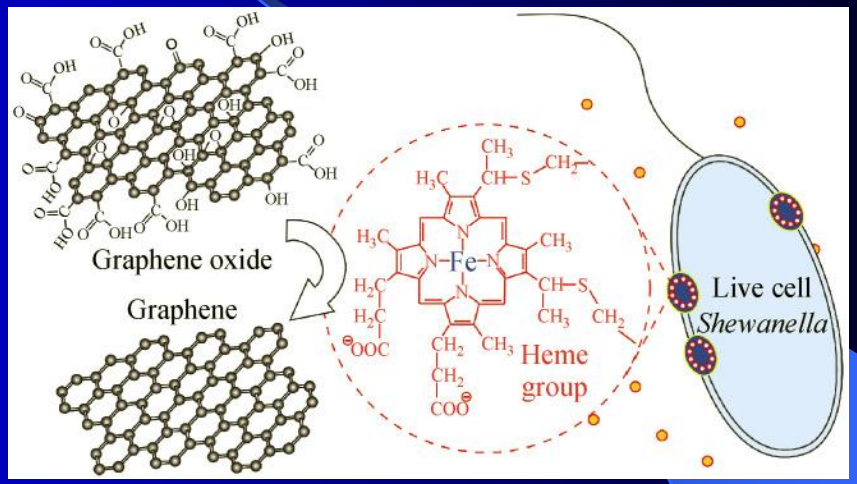
Yang, X., Shi, C., Wheeler, D., Newhouse, R., Chen, B., Zhang, J. Z. and Gu, C., J. Opt. Soc. Am. A 27, 977-984 (2010).

LCPCF SERS probe for aqueous bacteria detection



X. Yang, C. Gu, F. Qian, Y. Li, and J. Z. Zhang, Anal. Chem. **83**, 5888-5894 (2011).

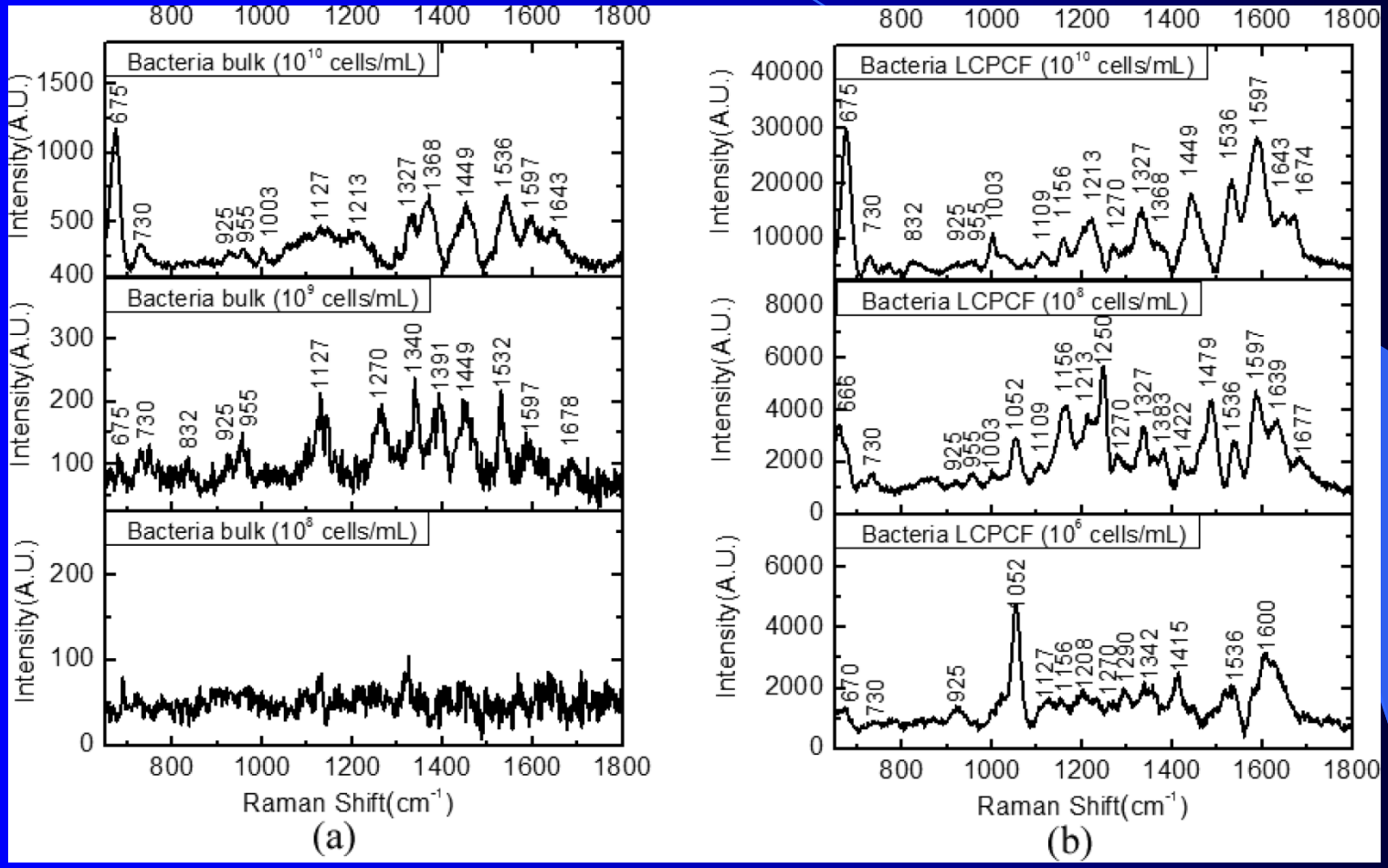
Shewanella oneidensis MR-1 cell



- Gram-negative facultative anaerobe
- Extracellular electron transfer capability
- Various applications:
  bioremediation of contaminated soils
  heavy metal detoxification
  microbial fuel cells
  microbial reduction of graphene oxide

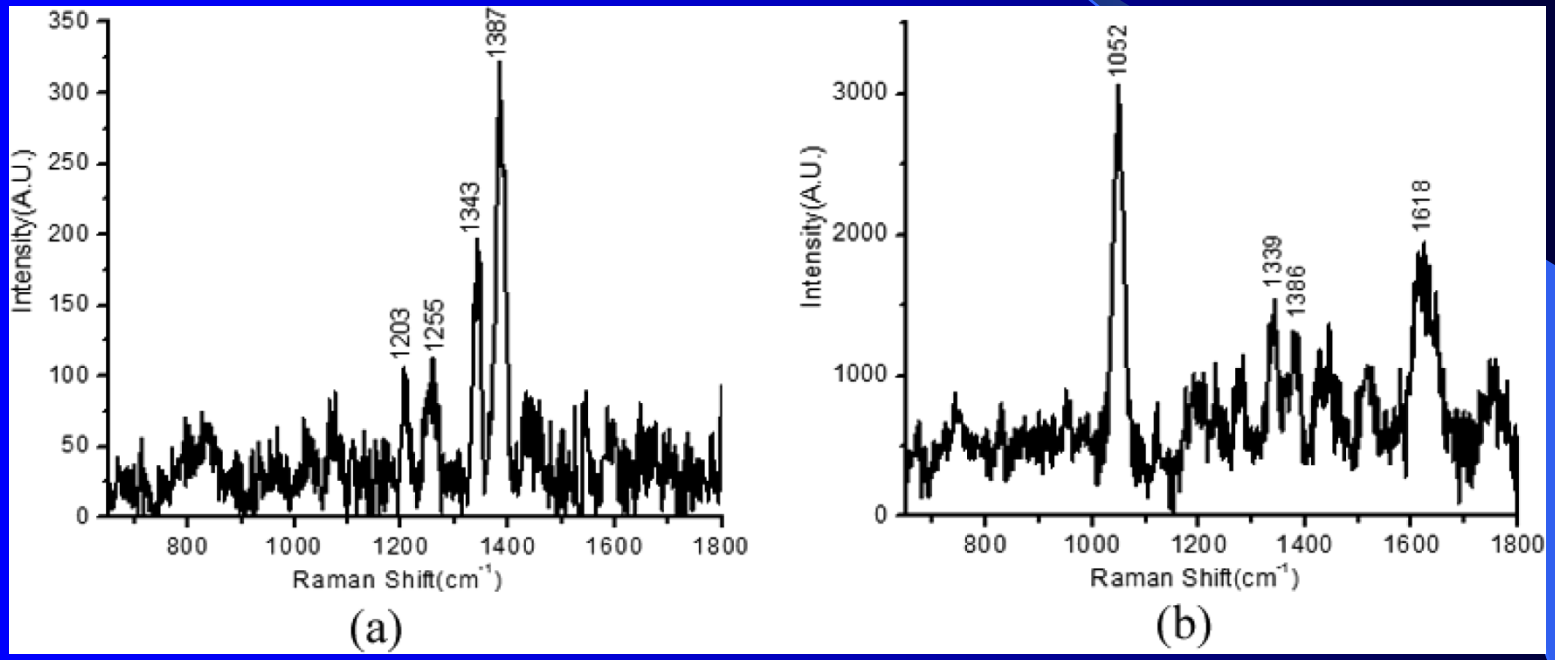
1) F. Qian *et al*., *Nano Lett.* **10**, 4686-4691 (2010)
2) F. Qian *et al*., *Biores. Technol*. **102**, 5836-5840 (2011)
3) G. Wang *et al*., *Nano Res*. **4**, 563-570 (2011)

LCPCF SERS probe for aqueous bacteria detection



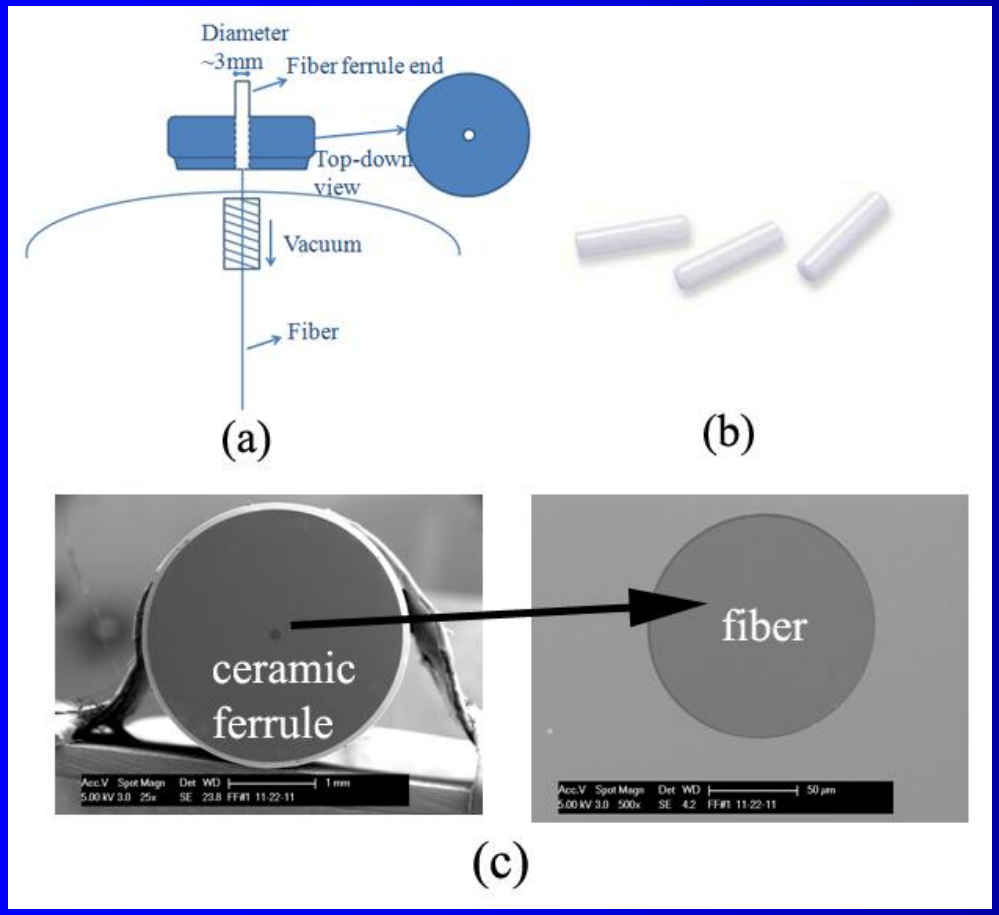
X. Yang, C. Gu, F. Qian, Y. Li, and J. Z. Zhang, Anal. Chem. **83**, 5888-5894 (2011).

Control experiments for aqueous bacteria detection



Control experiment with lactate medium and SNPs but without MR-1 cells (a) in bulk detection and (b) using the LCPCF SERS probe.

Nanopillar Array on a Fiber Facet – Fabrication



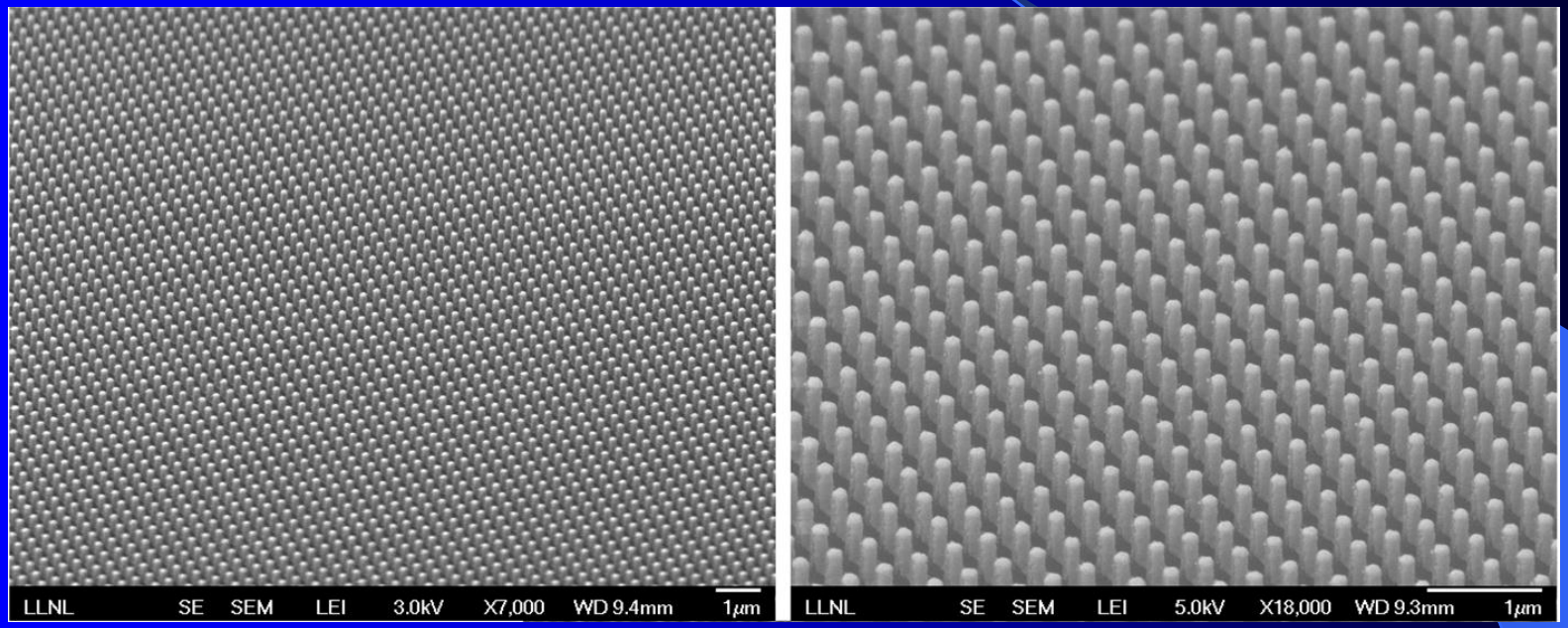
(a) Schematic of the spin coating process for the optical fiber sample

(b) Photograph of the fiber ferrule;

(c) SEM images of the fiber ferrule facet.

X. Yang, N. Ileri, C. C. Larson, T. C. Carlson, J. A. Britten, A. S. P. Chang, C. Gu, and T. C. Bond, "Nanopillar array on a fiber facet for highly sensitive surface-enhanced Raman scattering," *Opt. Exp*. **20(22)**, 24819-24826 (2012).

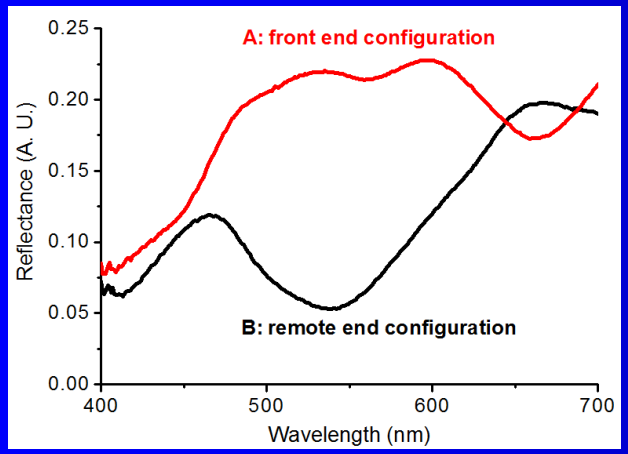
Nanopillar Array on a Fiber Facet – SEM Image



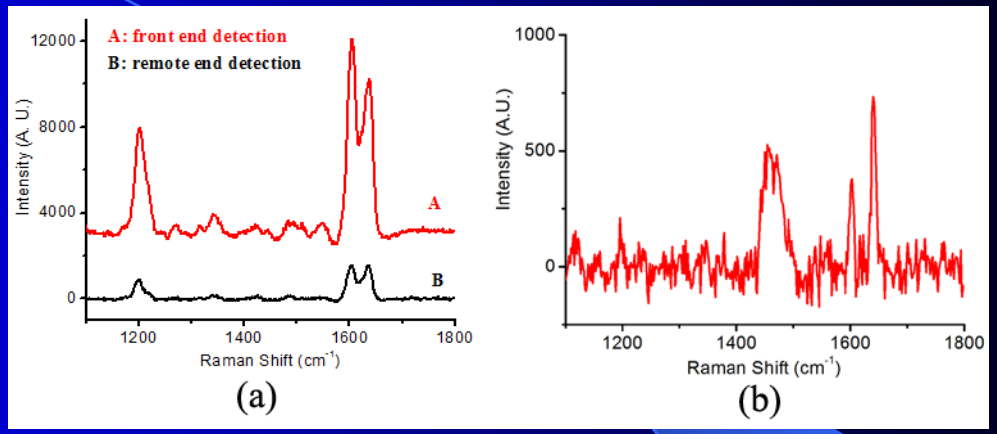
SEM images of the silver-coated nanopillar array patterned on the fiber core (tilted view: 45º)

X. Yang, N. Ileri, C. C. Larson, T. C. Carlson, J. A. Britten, A. S. P. Chang, C. Gu, and T. C. Bond, "Nanopillar array on a fiber facet for highly sensitive surface-enhanced Raman scattering," *Opt. Exp*. **20(22)**, 24819-24826 (2012).

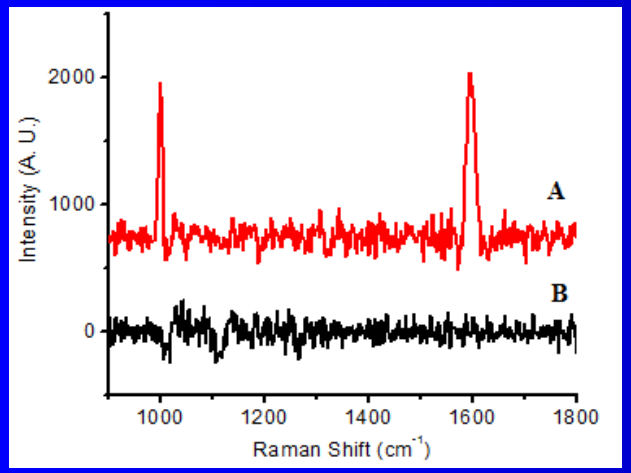
Results



Reflectance spectra of the fiber SERS probe in both the front end configuration (A) and remote end configuration (B)

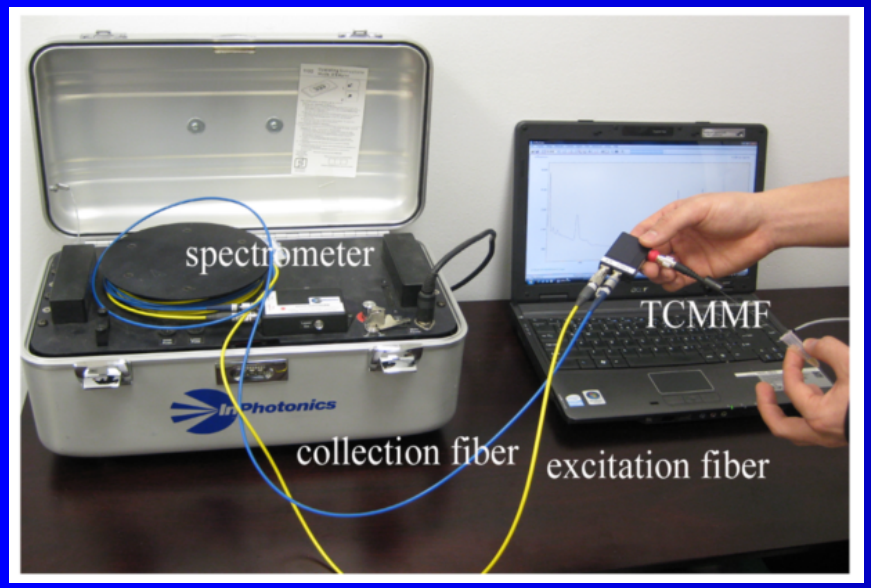


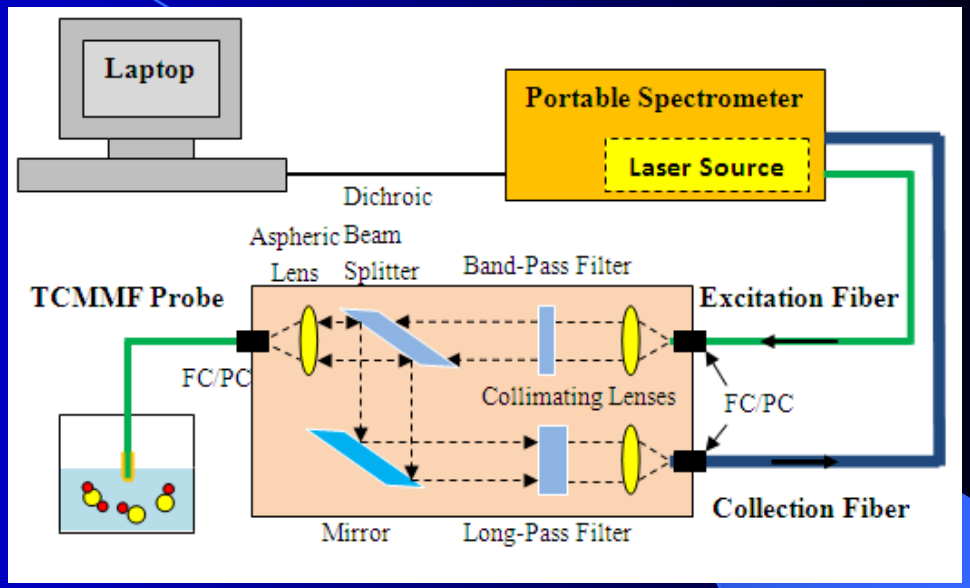
a) SERS spectra of BPE monolayer using the fiber SERS probe in both the front end configuration and remote end configuration (laser power: 0.2 mW, integration time: 10 s); (b) Raman spectrum of 0.1 M BPE obtained with the same spectroscopy system (laser power: 2 mW, integration time: 10 s).



Curve A: the SERS spectrum of the fiber probe for the remote detection of toluene vapor (laser power: 2 mW, integration time: 10 s); Curve B: the spectrum obtained by the unpatterned optical fiber in the toluene vapor with the same system configuration.

Integrating the TCMMF SERS probe with a portable Raman spectrometer

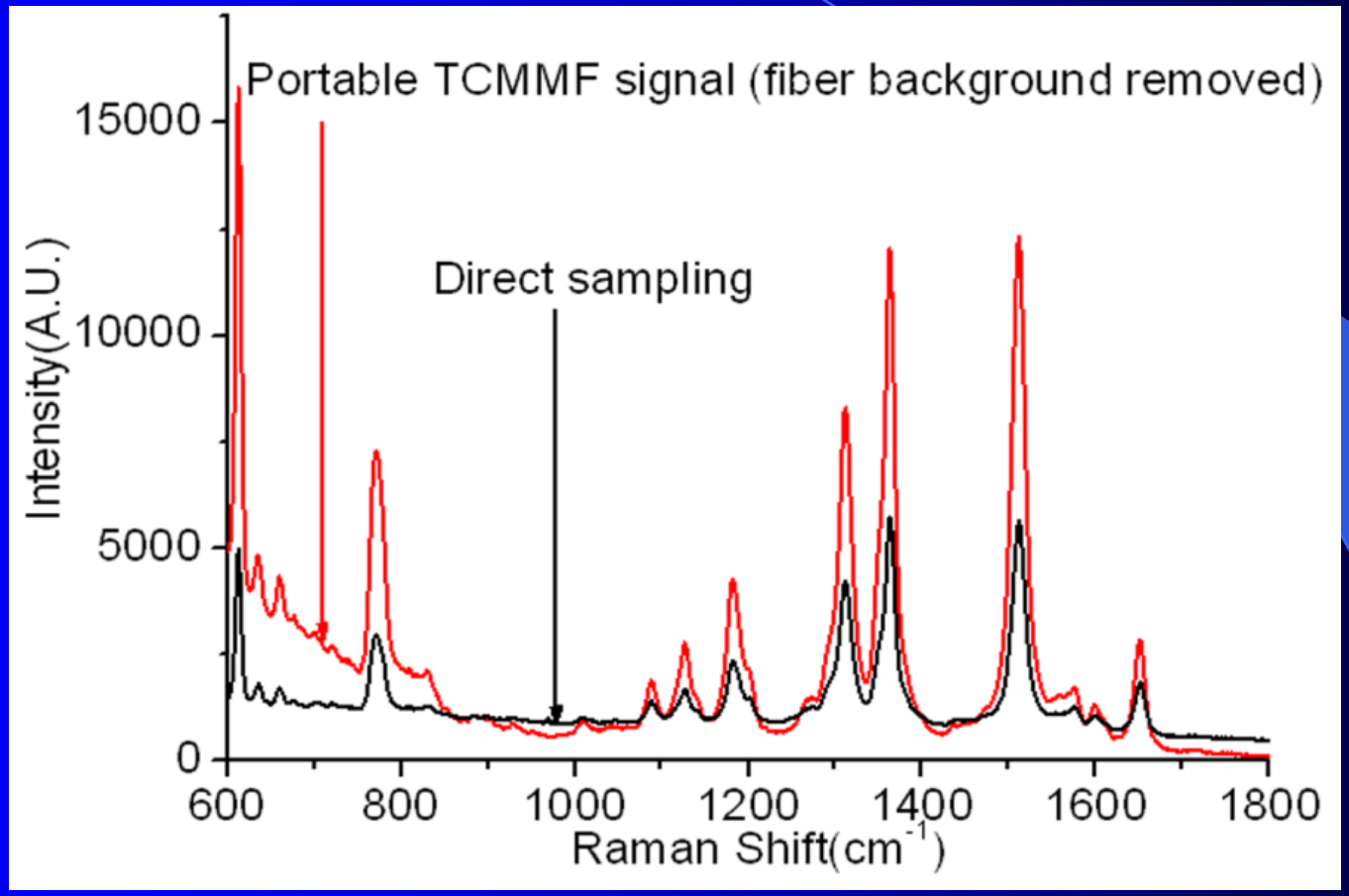




- TCMMF provides 2-3 times stronger SERS signal than direct sampling, similar to the result under the bulky Renishaw Raman system
- Flexible and alignment free
- The SERS probe is reusable.

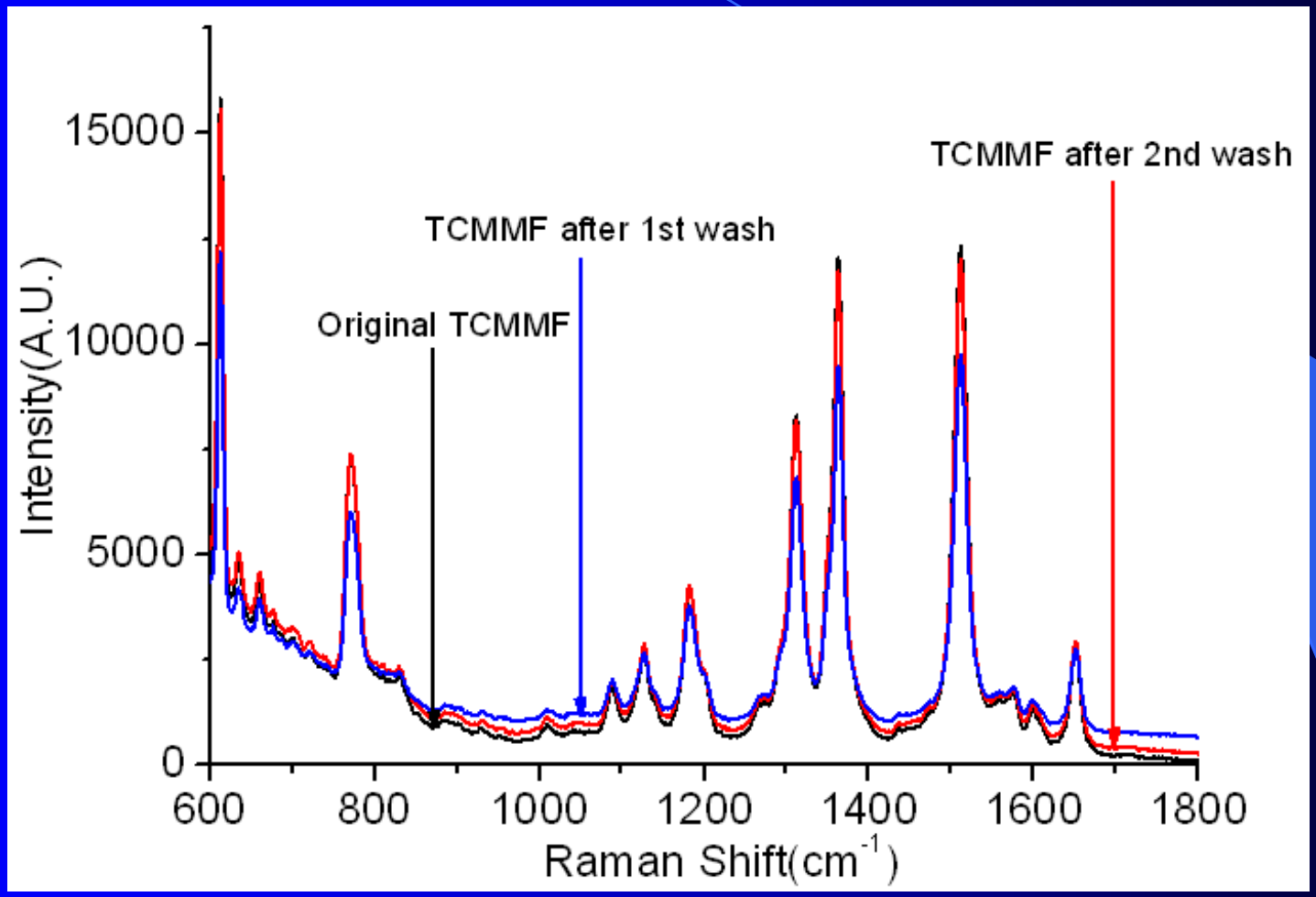
X. Yang, Z. Tanaka, R. Newhouse, Q. Xu, B. Chen, S. Chen, J. Z. Zhang, and C. Gu, Rev. Sci. Instrum. **81**, 123103 (2010).

Result from the TCMMF-portable SERS system



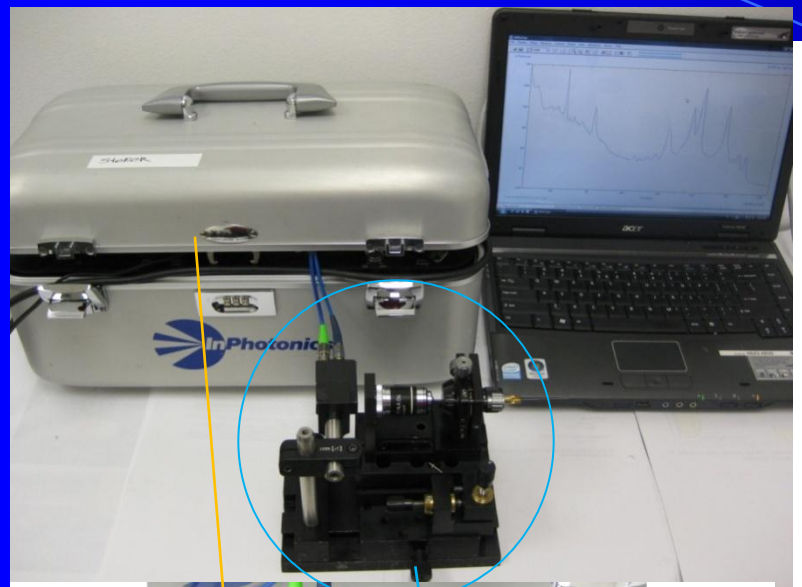
SERS signals obtained using the portable-TCMMF system and that obtained using direct sampling, when the R6G concentration is 10^{-5} M

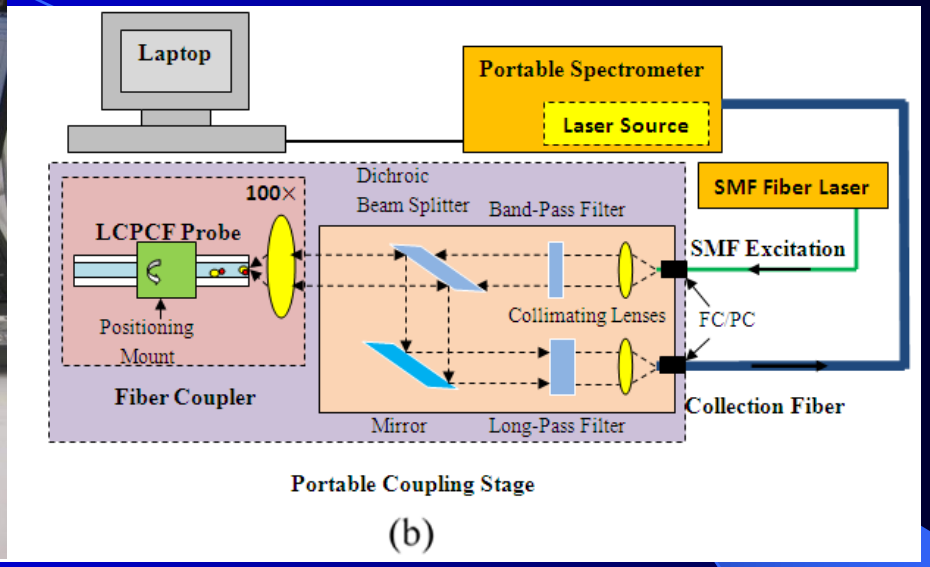
Reusability of the TCMMF SERS probe



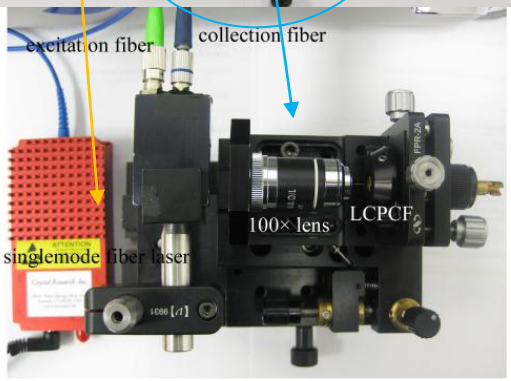
SERS signals obtained using the portable-TCMMF system after washing procedures.

Portable LCPCF SERS Sensor System

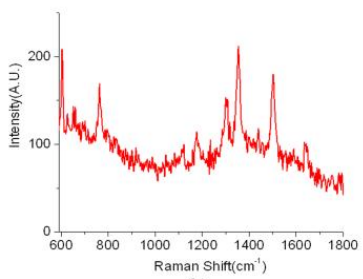


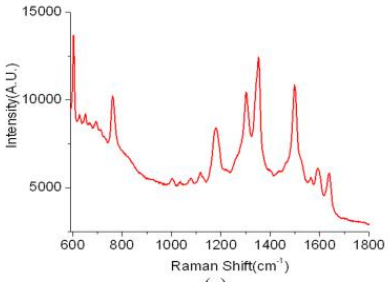


(b)



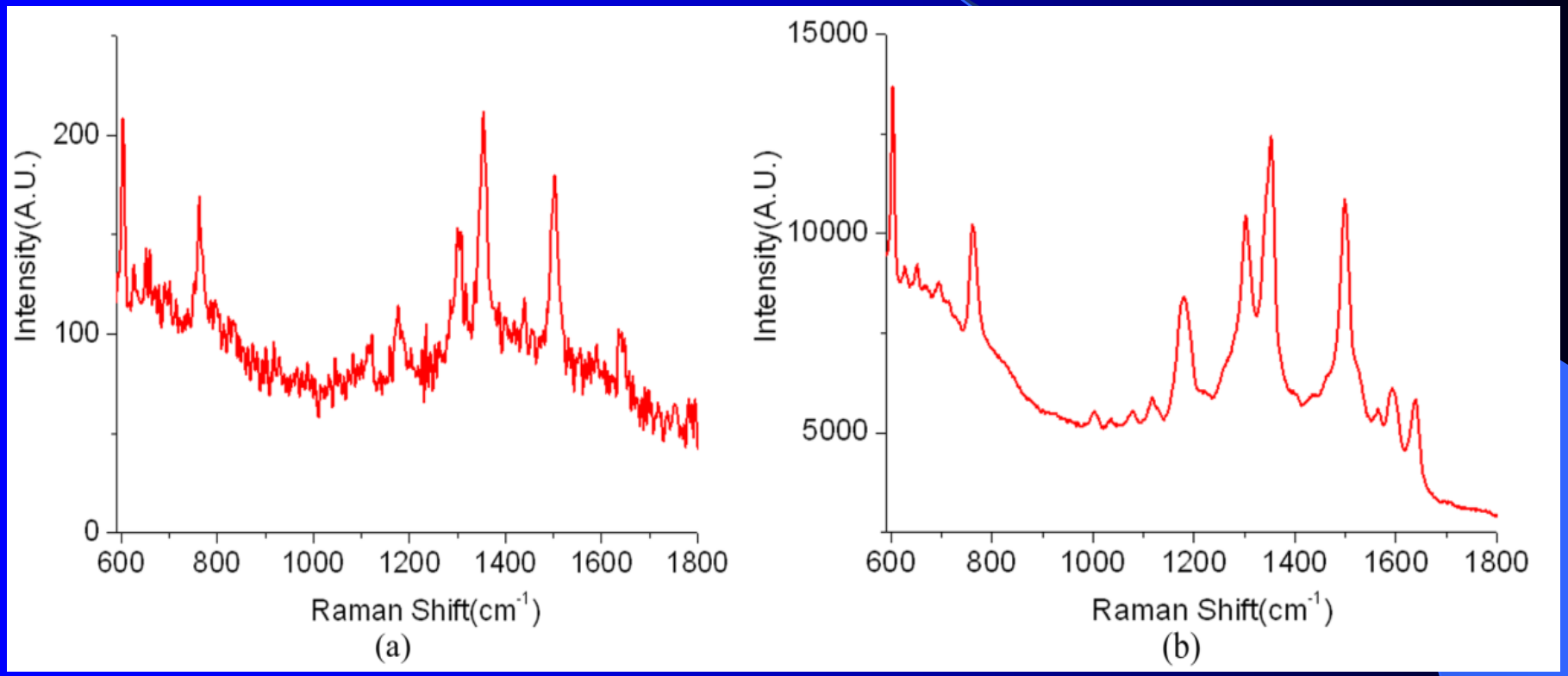
(a)





- No optical table or breadboard
- Real-time adjustment
- Portable
- Sensitivity enhancement (59 times stronger SERS signal than direct sampling)

Result from the LCPCF-portable SERS system



SERS signals obtained using (a) direct sampling, and (b) the portable-LCPCF system, when the R6G concentration is 10^{-6} M.

Conclusion

- Optical Fibers as a Platform for Chemical Sensors
  - Fibers – additional sensitivity enhancement (beyond interconnects)
  - Tip-Coated Multimode Fibers (TCMMF)
  - Liquid Core Photonic Crystal Fiber (LCPCF)
  - Nanostructured Optical Fiber
  - Integrated Portable Sensor System
  - Chemical, biomedical, and environmental applications
- Fiber-based SERS sensors provide a compact, low-cost, non-invasive optical technique with unique combination of molecular specificity and extremely high sensitivity for potential chemical and biomedical applications