Nanogap-Enhanced Raman Scattering (NERS)

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Raman scattering can provide a wealth of molecular chemical information, but it is basically a highly inefficient inelastic light scattering process between photon and molecule with a very small cross-section. Raman scattering signals are often poorly reproducible, meaning that very strong and controllable amplification mechanism, such as SERS(Surface-Enhanced Raman Scattering), TERS(Tip-Enhanced Raman Sccatering), or NERS(Nanogap-Enhanced Raman Scattering), is needed to obtain measurable and reliable signals [1-2].

Started from the simple wet-chemical nanogap generation induced by Coulomb aggregation among colloidal nanoparticles in aqueous solution after adding salt onto it shown independently by S. Nie and K. Kneipp in 1997, nanogap engineering to enhance Raman scattering signal to achieve single molecule sensitivity is getting more sophisticated [1].

Plasmonically coupled metallic nanostructures with ultra-small (~1 nm or smaller) nanogaps can generate very strong and controllable electromagnetic fields that can generate strong NERS signals from Raman dyes inside the nanogap. Therefore, plasmonic nanogap-enhanced Raman scattering (NERS) can be defined as Raman scattering signal enhancement from plasmonic nanogap with ~1 nm gap size.

In this talk, I will overview recent breakthroughs, advances, application, and prospects of plasmonic nanogap-enhanced Raman scattering with metal nanogap particles revealed by single-molecule/single-particle-level Nano Raman spectroscopy showing that these plasmonic nanogap particles can generate ultra-strong, quantifiable Raman signals in a highly reproducible manner. Specifically, single molecule Surface-Enhanced Raman Scattering (smSERS) field formed since 1997 will be briefly reviewed [1] and then different types of nanogap engineering strategy for smSERS developed in my lab will be discussed: single-junction 0-D external nanogap between two spherical nanoparticles connected with a double helix DNA [3-6], multi-junction 3-D spherical nanogap internally formed between spherical gold core nanoparticle and spherical gold shell nanoparticle connected by multiple single helix DNAs [7], and 2-D nanogap arrays formed on a 4-inch polymer wafer by simple two-step process. Several reasons will be discussed why now SERS regime and NERS (Nanogap-enhanced Raman Scattering) regime should be separated

on the enhancement factor (EF) distribution histogram. Recent result including direct near-field visualization of the nanogap field of the 2-D nanogap array, single molecule behavior of cytochrome C protein's Raman signal, and ultra-uniform distribution of SERS enhancement factor (EF) of benzene thiol molecule dispersed on this plasmonic 2-D nanogap array wafer will be presented [8]. In the latter part of my talk, I will briefly overview another research field of my research group, "Live Cell & *in vivo* Imaging based on UCNPs (Up-Converting Nano Particles)", which is a main topic of recently awarded GRL(Global Research Lab) Project of NRF(National Research Foundation), Korea, working with Columbia University [9-12].

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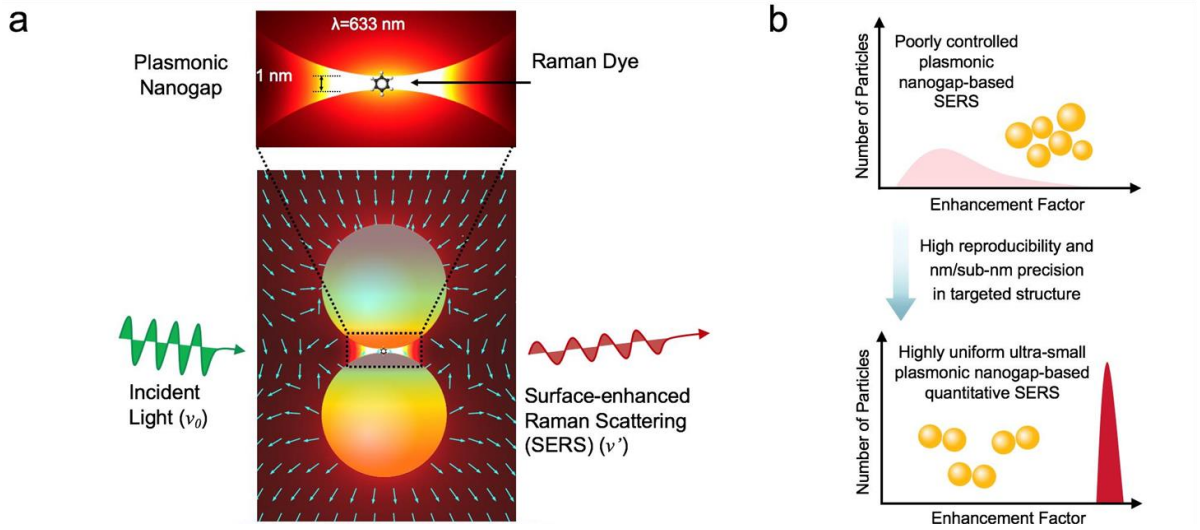
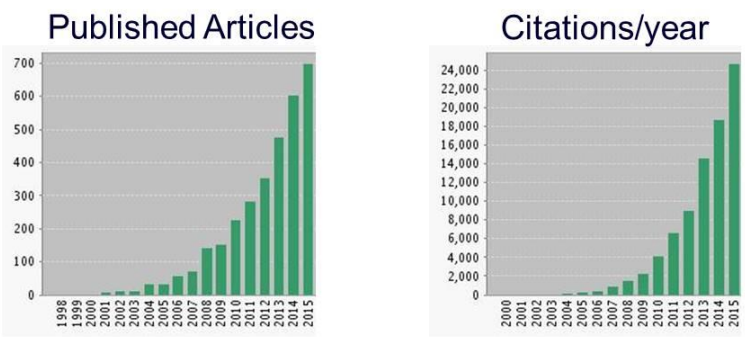


Figure 1 (a) Highly-enhanced electromagnetic (EM) fields in the 1 nm gap of a plasmonic dimer, **(b)** Fulfilling BOTH high surface-enhanced Raman scattering (SERS) enhancement factor (EF) AND narrow EF distributions to make SERS signals detectable, linear, thus quantitative, toward practical real-world biomedical/clinical applications like in the case of UV-Vis absorption or fluorescence emission.

Probes for Luminescence Bio Imaging

Ideal properties	Organic Dye Molecule	Fluorescent Proteins (GFP)	Quantum Dots	UCNPs
Brightness	✡✡✡	✡✡✡	✡✡✡	✡✡✡
Photostability (nonbleaching)	x		✡✡	✡✡✡
Emission continuity (nonblinking)				✡✡✡
Lack of overlap with cellular autofluorescence	✡	✡	✡✡	✡✡✡
Near-IR (deep penetration)		x	✡✡	✡✡✡
Biocompatibility	✡✡	✡✡✡	x	✡✡✡
Multimodal Imaging	x	x	✡✡	✡✡✡



Statistics for "upconverting nanoparticles" (ISI Web of Science)

Figure 2 (a) UCNP as an ideal bio-imaging probe. **(b)** Annual publications and citations of UCNP.

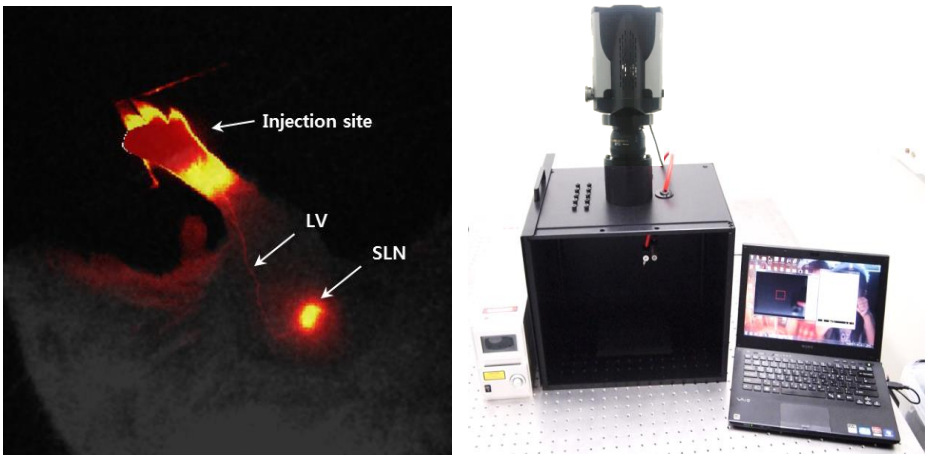


Figure 3 (left) *in-vivo* sentinel lymph node (SNL) optical imaging of Balb/C mouse after injection of Tm^{3+}-doped UCNPs. **(right)** Home-made Near-IR *in-vivo* imaging system for UCNP, developed by RC^2NT, KRICT.