Front. Phys., 2014, 9(1): 25–30
DOI 10.1007/s11467-013-0338-4

REVIEW ARTICLE

Single-molecule surface-enhanced Raman scattering: Current status and future perspective

Zee Hwan Kim

Department of Chemistry, Korea University, Seoul 136-701, Korea
E-mail: zhkim@korea.ac.kr

Received April 3, 2013; accepted April 19, 2013

The single-molecule surface-enhanced Raman scattering (smSERS) has been extensively studied after the initial observation in 1997, yet there still exist unsettled issues in the fundamental mechanism of smSERS. In this review, we survey some of the recent breakthroughs in the mechanism of smSERS and its application.

Keywords plasmonics, nanoparticles, molecular vibration, Raman scattering

PACS numbers 71.45.Gm, 78.30.Jw

Contents

1 Introduction

After the first discovery of the surface-enhanced Raman scattering (SERS) by Fleischman and co-workers [1], and by Jeammaire and Van Duyne [2], the mechanistic studies of SERS continues to be the topic of active research [3–5]. A major breakthrough in SERS came along in the reports by Nie and Emory [6], and Kneipp *et al.* [7], in which they claimed that they measured the SERS signal of a single or a few organic dye molecules (hereafter called smSERS). These reports, together with many others that followed, revitalized the SERS studies, and has promised that the smSERS may become another optical spectroscopic tool that is as sensitive as, or even better than, the single-molecule fluorescence (smF). What then now remains to be discovered for the mechanisms of smSERS? Why is it that the smSERS has not yet been fully utilized for the chemical and biochemical applications? In this article, we briefly review what has been newly discovered and what still remains uncertain.

2 Generic signature of smSERS

The key observations by Nie and Emory [6], Kneipp *et al.* [7] are the temporal fluctuation in SERS intensities and spectral diffusion [see Figs. 1(b) and (c)]. In addition, the intensity fluctuation appears to follow Poisson distribution. All of these observations are analogous to those of the fluorescence signal from a single dye molecule. The enhancement factor (EF), the ratio of SERS signal versus normal Raman signal, of such site is estimated to be as large as 10^{14}. Figure 1(a) sketches widely accepted view of SERS hotspot responsible for such smSERS [8–10]. Two or more metallic nanoparticles (Ag or Au) that are separated by d (typically less than a nanometer) produce strongly enhanced local field (E_{loc}) at the gap when resonantly driven by incident light (E_0). If the target molecule is placed at or nearby such junctions, the molecule generates strongly enhanced Raman-shifted field, and it again excites the electromagnetic modes of such metallic aggregates, producing the SERS signals at far-field. Such gap-field and associated resonance can explain at least 10^{10} fold enhancement of the observed SERS signals. The rest of the missing 10–1000 fold enhancement is usually attributed to the non-plasmonic (or chemical) effects, which includes the changes in static and dyanamic polarizability

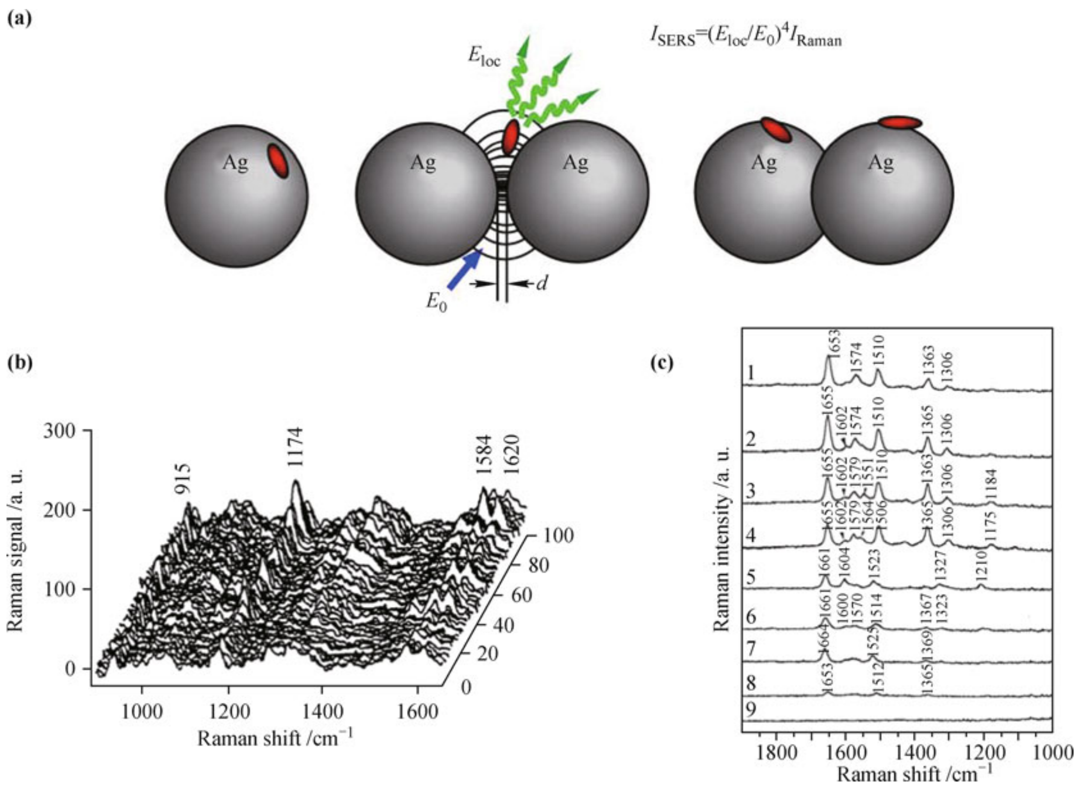

Fig. 1 **(a)** Generic structure of gap-plasmon SERS hotspot. **(b)** Time-resolved SERS trajectory of crystal violet molecules adsorbed on silver nanoparticles [7]. **(c)** Time-resolved SERS trajectory of R6G molecules adsorbed on silver nanoparticles [6]. Copyright © American Physical Society, and the American Association of Advancement of Science.

tensors of molecules, vibronic charge transfer between the molecules and metallic surfaces, and molecular electronic resonances [3–5]. Based on the above consideration, one should be able to design and fabricate a various forms of gap structures (such as dimeric nanoparticles, bow-tie antenna structures, or nanosphere-thin film assemblies) with smallest possible (small enough to accommodate one or a few molecules) gap distance. The experimental realization of such controlled-junction structure is still a major challenge for nano-engineering, yet it is within the reach of current technology. Besides such fabrication issue of nano-gap structures, there exist a few fundamental issues regarding the genuine signature of sm-SERS, which we discuss below.

3 Re-examination of single-molecularity of smSERS

To fully understand the difficulty of "counting" the number of molecules with SERS signals, we need to understand several intrinsic complexities unique to the SERS and smSERS signals. First, the SERS signals do not usually yield clear-cut "quantized" signal intensities as is routinely found in the single-molecule fluorescence trajectories. This is mainly due to the fact that the local field intensities and hence the SERS signals critically depend on the detailed geometries of the metallic nanostructures, and also on the exact location of the molecules with respect to the hotspot [4]. As such, two identical molecules at different sites yield drastically different signal intensities. Secondly, the SERS signal also accompanies a continuum emission (so-called SERS continuum) [11], the origin of which still remains uncertain. Thirdly, the organic molecules adsorbed on metallic surfaces often undergo surface-assisted photo-reactions and generate carbonaceous products with large Raman cross sections, which strongly interferes with the native SERS spectra of target molecules. As such, the temporal fluctuation of SERS spectra alone is not a sufficient evidence to claim the true smSERS [12]. Furthermore, it was recently pointed out [13] that the original Poisson-like intensity distribution observed by Kneipp *et al.* [7] is likely to be a statistical artifact, rather than the genuine signature of SERS signals of a single or a few molecules.

To critically re-examine the single-molecularity of the SERS signals, Le Ru *et al.* [14], and Van Duyne coworkers [15] have developed an analysis method called the bi-analyte technique (see Fig. 2): two species with similar surface sticking coefficients and Raman cross sections (called A and B) are co-adsorbed on the SERS substrate, and the temporal evolution of the SERS spectra is monitored. If the SERS hotspot can accommodate only one molecule, the SERS spectra will reflect either those of pure A or pure B, but not those of the mixture of the two. On the other hand, if the hotspot accommodates many A and B molecules, the SERS trajectory in most of the time will show the mixed spectra of the A and B. They unambiguously proved the single-molecularity of SERS signals. Based on this method, they also showed that the enhancement of 10^9 is sufficient [16] for the smSERS of nonresonant molecules such as adenines, which is much lower value than has been originally believed value of 10^{14}.

4 Refined assessment of enhancement mechanisms of smSERS

There is no doubt that the plasmonic EM-enhancement plays a dominant role in SERS and smSERS. This naturally generates a general impression that the SERS excitation spectrum, i.e., the SERS signal as a function of excitation wavelength (λ_{ex}), will be similar to that of (far-field) plasmon scattering spectra (such as dark-field scattering spectra or transmission spectra). This simplified view of EM-enhancement is, however, not entirely correct because the SERS is a near-field effect whereas the dark-field scattering or transmission spectra sample only the far-field component of the light-matter interaction. Van Duyne and co-workers [17] recently reported a striking difference between the SERS excitation and the far-field spectra of a single dimeric SERS structure, which disproves the generally accepted belief on the excitation wavelength dependence in SERS and smSERS.

Another important aspect of the EM-enhancement is the possible role of quantum mechanical plasmonic tunneling in SERS. In generic SERS structures as shown in Fig. 1, the nanostructures are usually separated by 1 nm or less. As such, the oscillating plasmonic electrons may tunnel through the junction and through the target molecule. This may change the plasmon resonance frequencies and reduces the local field intensities. Such possibility was first pointed out by Zuloaga *et al.* [18]. Baumberg and co-workers [19] recently reported the significant deviation of experimental resonance spectra and classical electrodynamics theory at very small gap distance, which show the existence of quantum plasmonic tunneling. Currently, it is still not clear to what extent this quantum tunneling will influence the SERS and

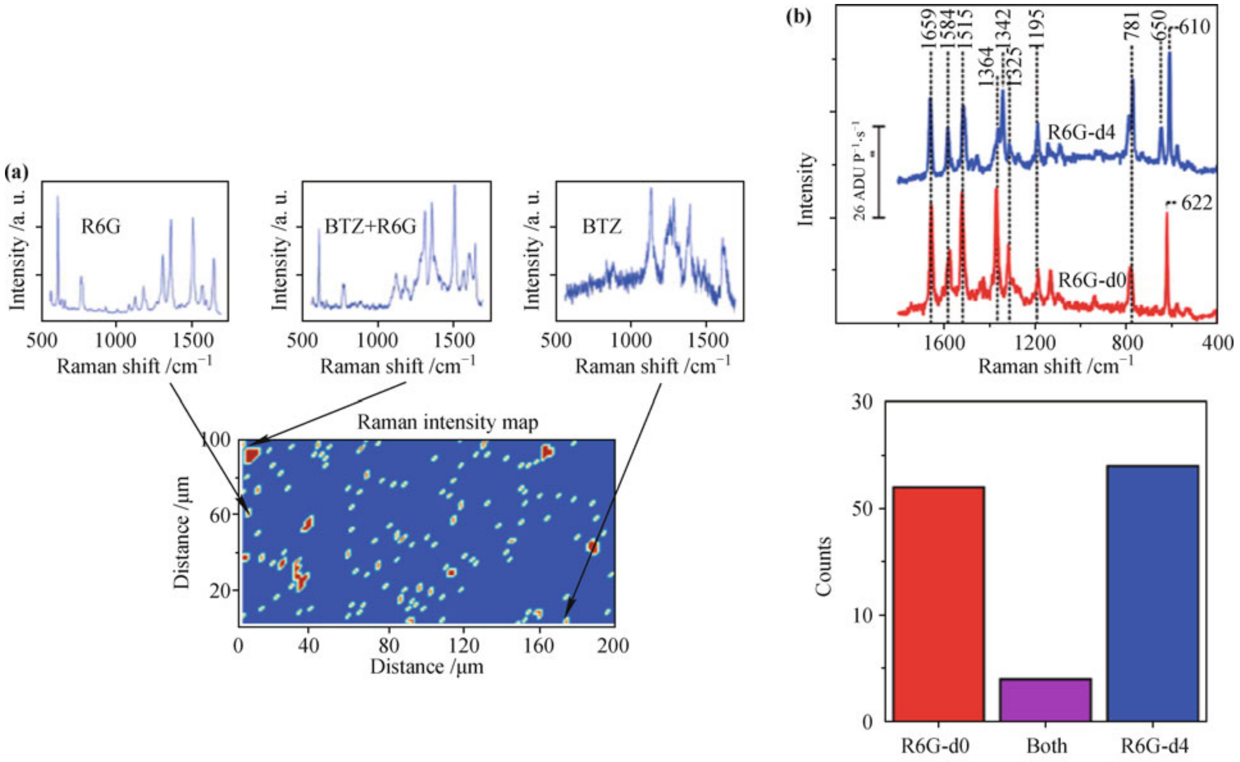

Fig. 2 **(a)** SERS microscopy image and spectra showing single-molecule events and mixed events [14]. **(b)** *Top-panel*: smSERS of mixture of R6G-h6 and R6G-d6. *Bottom-panel*: Histogram of peak occurrence [15]. Copyright © American Chemical Society.

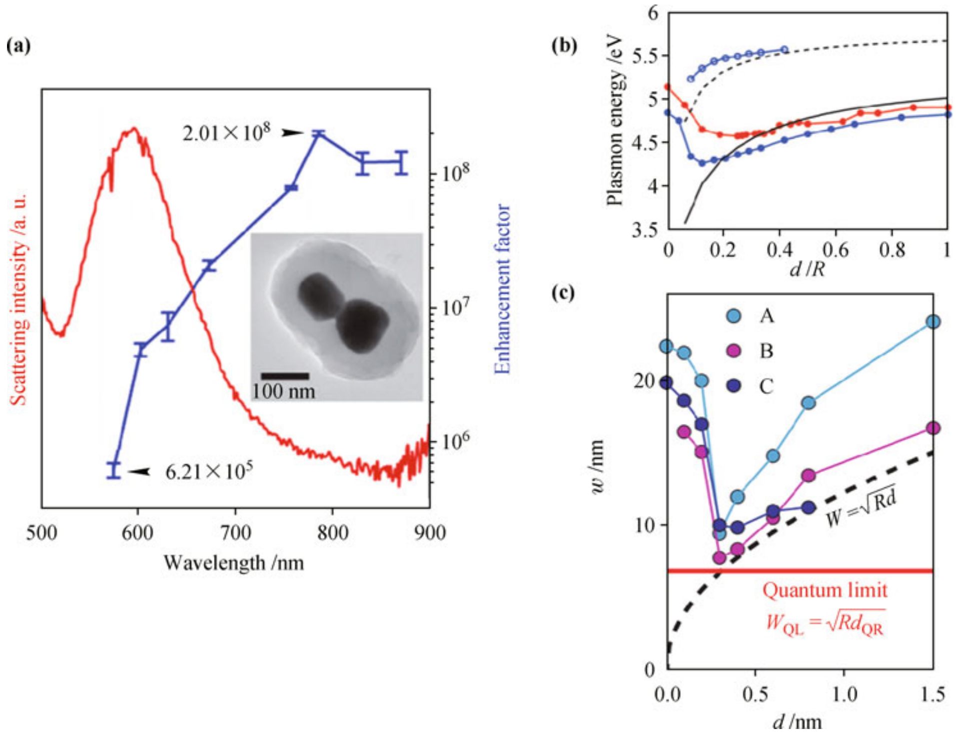

Fig. 3 **(a)** SERS excitation spectrum versus far-field scattering spectrum of a dimeric SERS hotspot [17]. **(b)** Quantum theory prediction of plasmon energy as a function of gap-distance in dimeric nanoparticle [18]. **(c)** Experimental field confinement (w) as a function of gap-distance in nanoparticle dimer system [19]. Copyright © American Chemical Society, Nature Publishing Group.

smSERS intensities.

5 Chemical enhancement

The role of chemical-enhancement (or more specifically the charge-transfer (CT) enhancement), in smSERS is still poorly understood as compared with that of EM-enhancement. The major difficulty of assessing the CT-enhancement in SERS and smSERS arise from the difficulty of disentangling the CT-enhancement from those of re-orientation of molecules and adsorption/desorption of molecules, which may depend on the chemical potential of metallic surfaces (i.e., electrochemical potential of the metallic surfaces). Furthermore, it was recently pointed out that some of the standard CT-enhanced peaks in SERS may be an artifact of photochemical reaction [20, 21], which add another complexity in understanding the role of CT-enhancement. Lombardi *et al.* [22] recently summarized the current view of CT-enhancement in smSERS.

6 Application of smSERS

While the details of the mechanisms of smSERS need further studies, it is now clear that properly designed plasmonic gap junctions provide sufficient enhancement for routine smSERS measurements. An obvious next step is the application of smSERS for investigating the chemical and biochemical reactions. The smSERS or SERS require the target molecules to be placed at or nearby the metallic surfaces. As such, the most natural application of SERS and smSERS is monitoring the surface chemical reactions involving metal-molecule interactions, including metal-molecule charge-transfer reaction, oxidation/reduction cycles [23], and plasmon-assisted reactions [24]. Sun *et al.* [25], and Landman *et al.* [26] employed the tip-enhanced Raman scattering (TERS) to monitor the chemical reactions occuring at a single hotspot. Xie *et al.* [27] fabricated a hybrid nanostructure that combines the plasmonic and catalytic activities and successfully monitored the surface catalytic reactions using SERS. Cortes *et al.* [23] combined the electrochemistry and smSERS to observe the redox cycles of a single molecule.

Another important application of smSERS and SERS is the combined measurement of molecular conductivity and SERS of a single molecule [28–30]. There are at least three reasons why such combined measurement is important. First, as in smSERS, a genuine single-molecularity in sm-conductivity has been a subject of intense debate and combined SERS and conductivity measurement can provide a resolution to this issue [28]. Second, the SERS can provide complementary information on the molecular structures, state of metal-molecule contact, and molecular orientation, most of which are not directly accessible from the conductivity measurement alone [29]. Thirdly, the SERS can provide an important answer to the question on the vibronic interaction between the tunneling electrons and the molecular vibrations, which is of fundamental interest in the field of chemical and molecular physics in general [30].

7 Summary and conclusion

In this article, we have reviewed recent breakthroughs in smSERS and SERS. It is now clear that, with properly designed plasmonic gap structures, one can measure the SERS of individual molecules. Many details of smSERS mechanism, including the possible role of quantum tunneling and chemical enhancement, still remain to be subjects of further studies. Nevertheless, the smSERS is now mature enough to be applied to many other related disciplines such as surface chemistry and molecular electronics. We expect that more unforeseen applications of smSERS will emerge in the near future.

Acknowledgements Z. H. Kim acknowledges the financial support (Grant Nos. 2012-0005860, 2012-0006218, 2012-0008686, and 2012-0000606) from the National Research Foundation of Korea (NRF) funded by the Ministry of Education, Science and Technology (MEST).

References

1. M. Fleischmann, P. J. Hendra, and A. J. McQuillan, Raman spectra of pyridine adsorbed at a silver electrode, *Chem. Phys. Lett.*, 1974, 26(2): 163
2. D. L. Jeanmaire and R. P. Van Duyne, Surface Raman spectroelectrochemistry, *J. Electroanal. Chem.*, 1977, 84(1): 1
3. M. Moskovitz, Surface-Enhanced Raman Scattering: Physics and Applications, Topics in Applied Physics, Vol. 103, Heidelberg: Springer, 2006
4. E. C. Le Ru and P. G. Etchegoin, Single-molecule surface-enhanced Raman spectroscopy, *Annu. Rev. Phys. Chem.*, 2012, 63(1): 65
5. K. A. Willets and R. P. Van Duyne, Localized surface plasmon resonance spectroscopy and sensing, *Annu. Rev. Phys. Chem.*, 2007, 58(1): 267
6. S. Nie and S. R. Emory, Probing single molecules and single nanoparticles by surface-enhanced Raman scattering, *Science*, 1997, 21(5303): 1102
7. K. Kneipp, Y. Wang, H. Kneipp, L. T. Perelman, I. Itzkan, R. R. Dasari, and M. S. Feld, Single molecule detection using surface-enhanced Raman scattering (SERS), *Phys. Rev. Lett.*, 1997, 78(9): 1667
8. F. J. García-Vidal and J. B. Pendry, Collective theory for surface enhanced Raman scattering, *Phys. Rev. Lett.*, 1996, 77(6): 1163
9. H. Xu and M. Käll, Polarization-dependent surface-enhanced Raman spectroscopy of isolated silver nanoaggregates, *ChemPhysChem*, 2003, 4(9): 1001
10. J. Jiang, K. Bosnick, M. Maillard, and L. Brus, Single molecule raman spectroscopy at the junctions of large Ag nanocrystals, *J. Phys. Chem. B*, 2003, 107(37): 9964
11. A. A. Moore, M. L. Jacobson, N. Belabas, K. L. Rowlen, and D. M. Jonas, 2D correlation analysis of the continuum in single molecule surface enhanced Raman spectroscopy, *J. Am. Chem. Soc.*, 2005, 127(20): 7292
12. K. F. Domke and B. Pettinger, Comment on "Scanning-probe Raman spectroscopy with single-molecule sensitivity", *Phys. Rev. B*, 2007, 75(23): 236401
13. P. G. Etchegoin, M. Meyer, and E. C. Le Ru, Statistics of single molecule SERS signals: is there a Poisson distribution of intensities? *Phys. Chem. Chem. Phys.*, 2007, 9(23): 3006
14. E. C. Le Ru, M. Meyer, and P. G. Etchegoin, Proof of single-molecule sensitivity in surface enhanced Raman scattering (SERS) by means of a two-analyte technique, *J. Phys. Chem. B*, 2006, 110(4): 1944
15. J. A. Dieringer, K. A. Lettan, Scheidt, and R. P. Van Duyne, A frequency domain existence proof of single-molecule surface-enhanced Raman spectroscopy, *J. Am. Chem. Soc.*, 2007, 129(51): 16249
16. E. J. Blackie, E. C. Le Ru, and P. G. Etchegoin, Single-molecule surface-enhanced Raman spectroscopy of nonresonant molecules, *J. Am. Chem. Soc.*, 2009, 131(40): 14466
17. S. L. Kleinman, B. Sharma, M. G. Blaber, A. I. Henry, N. Valley, R. G. Freeman, M. J. Natan, G. C. Schatz, and R. P. Van Duyne, Structure enhancement factor relationships in single gold nanoantennas by surface-enhanced Raman excitation spectroscopy, *J. Am. Chem. Soc.*, 2013, 135(1): 301
18. J. Zuloaga, E. Prodan, and P. Nordlander, Quantum description of the plasmon resonances of a nanoparticle dimer, *Nano Lett.*, 2009, 9(2): 887
19. K. J. Savage, M. M. Hawkeye, and A. G. Ruben Esteban, Borisov, J. Aizpurua, and J. J. Baumberg, Revealing the quantum regime in tunnelling plasmonics, *Nature*, 2012, 491(7425): 574
20. Y. F. Huang, H. P. Zhu, G. K. Liu, D. Y. Wu, B. Ren, and Z. Q. Tian, When the signal is not from the original molecule to be detected: chemical transformation of para-aminothiophenol on Ag during the SERS measurement, *J. Am. Chem. Soc.*, 2010, 132(27): 9244
21. H. K. Choi, H. K. Shon, H. Yu, T. G. Lee, and Z. H. Kim, b_2 peaks in SERS spectra of 4-aminobenzenethiol: A photochemical artifact or a real chemical enhancement? *J. Phys. Chem. Lett.*, 2013, 4(7): 1079

22. J. R. Lombardi, R. L. Birke, and G. Haran, Single molecule SERS spectral blinking and vibronic coupling, *J. Phys. Chem. C*, 2011, 115(11): 4540

23. E. Cortes, P. G. Etchegoin, E. C. Le Ru, A. Fainstein, M. E. Vela, and R. C. Salvarezza, Monitoring the electrochemistry of single molecules by surface-enhanced Raman spectroscopy, *J. Am. Chem. Soc.*, 2010, 132: 18034

24. S. Mukherjee, F. Libisch, N. Large, O. Neumann, L. V. Brown, J. Cheng, J. B. Lassiter, E. A. Carter, P. Nordlander, and N. J. Halas, Hot electrons do the impossible: Plasmon-induced dissociation of H_2 on Au, *Nano Lett.*, 2013, 13(1): 240

25. M. Sun, Z. Zhang, H. Zheng, and H. Xu, In-situ plasmon-driven chemical reactions revealed by high vacuum tip-enhanced Raman spectroscopy, *Scientific Reports*, 2012, 2: 647

26. E. M. S. Lantman, T. Deckert-Gaudig, A. J. Mank, V. Deckert, and B. M. Weckhuysen, Catalytic processes monitored at the nanoscale with tip-enhanced Raman spectroscopy, *Nat. Nanotechnol.*, 2012, 7(9): 583

27. W. Xie, C. Herrmann, K. Kömpe, M. Haase, and S. Schlücker, Synthesis of bifunctional Au/Pt/Au Core/shell nanoraspberries for in situ SERS monitoring of platinum-catalyzed reactions, *J. Am. Chem. Soc.*, 2011, 133(48): 19302

28. D. R. Ward, N. K. Grady, C. S. Levin, N. J. Halas, Y. Wu, P. Nordlander, and D. Natelson, Electromigrated nanoscale gaps for surface-enhanced Raman spectroscopy, *Nano Lett.*, 2007, 7(5): 1396

29. Z. Liu, S.-Y. Ding, Z.-B. Chen, X. Wang, J.-H. Tian, J. R. Anema, X.-S. Zhou, D.-Y. Wu, B.-W. Mao, X. Xu, B. Ren, and Z.-Q. Tian, Revealing the molecular structure of single-molecule junctions in different conductance states by fishing-mode tip-enhanced Raman spectroscopy, *Nat. Commun.*, 2011, 2: 305

30. D. R. Ward, D. A. Corley, J. M. Tour, and D. Natelson, Vibrational and electronic heating in nanoscale junctions, *Nat. Nanotechnol.*, 2011, 6(1): 33