Surface- and Tip-Enhanced Raman Spectroscopy in Catalysis

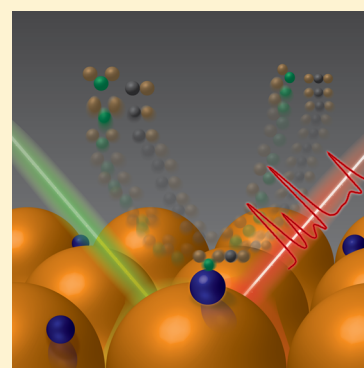Thomas Hartman,[†] Caterina S. Wondergem,[†] Naresh Kumar,[†,‡] Albert van den Berg,[§] and Bert M. Weckhuysen*,[†]

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ABSTRACT: Surface- and tip-enhanced Raman spectroscopy (SERS and TERS) techniques exhibit highly localized chemical sensitivity, making them ideal for studying chemical reactions, including processes at catalytic surfaces. Catalyst structures, adsorbates, and reaction intermediates can be observed in low quantities at hot spots where electromagnetic fields are the strongest, providing ample opportunities to elucidate reaction mechanisms. Moreover, under ideal measurement conditions, it can even be used to trigger chemical reactions. However, factors such as substrate instability and insufficient signal enhancement still limit the applicability of SERS and TERS in the field of catalysis. By the use of sophisticated colloidal synthesis methods and advanced techniques, such as shell-isolated nanoparticle-enhanced Raman spectroscopy, these challenges could be overcome.

Catalysis is essential in the field of sustainable chemistry because it allows reactions to take place more quickly, efficiently, and safely.[1−3] To improve chemical processes it is crucial to know how catalysts operate and how, why, and when they cease to work. Understanding the mechanism of all involved surface reactions in the case of heterogeneous catalysts is the key to designing the best possible catalytic materials. For this purpose, researchers use a wide variety of techniques. They originally used methods to study catalysts before and after reaction, such as spectroscopy, (electron) microscopy, and many more. Although these methods have greatly enhanced the understanding of catalysts, knowledge of actual *operating* catalysts remains incomplete. Understanding working catalysts requires the use of techniques that are able to identify when and where reactions take place, ultimately linking this information to the catalytic performance of these materials.

Valuable techniques for elucidating molecular structures are vibrational spectroscopy methods, including various forms of infrared (IR)[4−6] and Raman spectroscopy.[7−10] Raman spectroscopy enables the measurement of vibrational energy levels, which provide information about the molecular composition and structure within a sample. Operative under several different conditions, this spectroscopic technique has greatly improved the knowledge of both the syntheses[7,8] and operation[9,10] of catalytic solids. However, Raman spectroscopy lacks sensitivity due to the small Raman scattering cross section of analyte molecules.[11] The sensitivity of Raman spectroscopy can be enhanced using specialized techniques, of which resonance Raman,[11−14] coherent anti-Stokes Raman

spectroscopy (CARS),[15] and surface-enhanced Raman spectroscopy (SERS) are the three most popular choices.[16] All of these techniques have their own strengths and weaknesses, but compared to the others, SERS exhibits a strong feature for catalysis: highly localized sensitivity. This local sensitivity can be exploited to sense surface species and adsorbates.[17−19] Multiple techniques, such as CARS and SERS, can be combined to obtain even stronger signal intensities.[20]
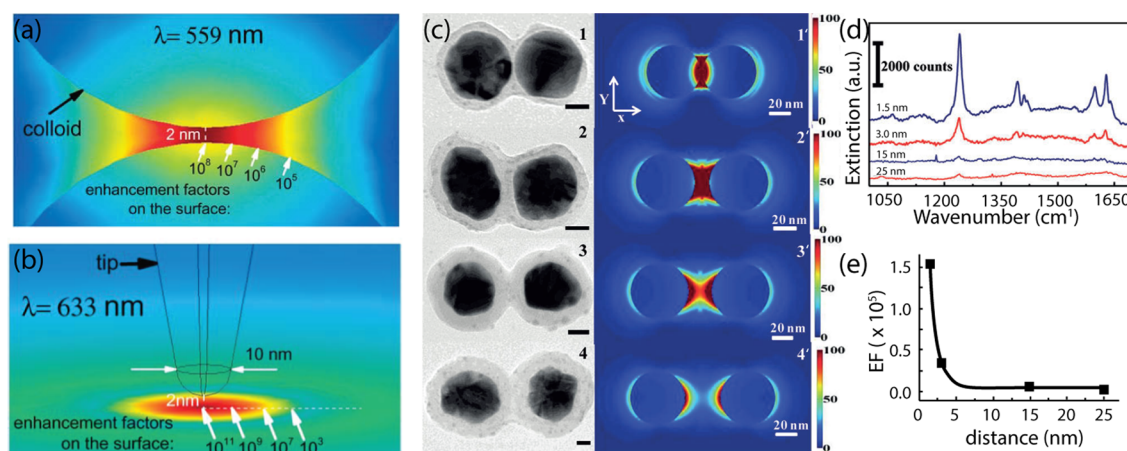
However, SERS is not the only surface-sensitive vibrational spectroscopic technique used in the field of catalysis. For example, other characterization techniques to study surface adsorbates include polarization modulation infrared reflection absorption spectroscopy (PM-IRRAS)[21,22] and sum frequency generation (SFG).[23−25] The latter approach has been pioneered by the group of Somorjai, and has been used, for example, to investigate the hydrogenation of benzene over platinum single crystals with a combined high-pressure scanning tunneling microscopy (HP-STM) and SFG instrument.[26] On the other hand, SERS enables the observation and characterization of the structure of surface species and adsorbates with greater sensitivity up to the level of detecting single molecules. When combined with scanning probe microscopy (SPM) methods, tip-enhanced Raman spectroscopy (TERS) can even reach nanoscale spatial resolution.[27] Furthermore, the SERS substrates can be triggered to start a reaction due to the formation of the strong electric field, hot

Figure 1. Strongest EFs arise from hot spots, which are produced by gap-mode plasmons that emerge between closely spaced plasmonic particles or tip−surface interactions where the plasmons overlap. (a) The Raman signal EF can reach theoretical values of 10^8 for dimer gold nanoparticles under 559 nm laser irradiance[40] and (b) 10^{11} for a sharp gold tip−gold surface interaction under 633 nm laser irradiance.[40] (c) The electric field is at its strongest when the particles touch and rapidly reduces to a negligible value when the particles are more than 15 nm away from each other. (d) This can be observed in the SERS spectra of adsorbed ammonium salt of pyrene on Ag@SiO$_2$ spheres. (e) Plot of SERS EF versus distance between the particles.[41] Reprinted with permission from ref 40. Copyright 2008 Royal Society of Chemistry. Reprinted from ref 41. Copyright 2012 American Chemical Society.

electrons, and the involved heat generation.[28,29] With increased control over these SERS substrates, improved Raman signals are obtained with shorter acquisition times, allowing the observation of possible reaction intermediates or even transition states.[30,31]

A few hurdles need to be overcome before SERS and TERS can become a routine analytical tool for catalysis. In this Perspective, we briefly introduce the capabilities and challenges of SERS and TERS and present several examples of past work and future perspectives to encourage readers to start working with and expand the knowledge of these powerful analytical tools for the study of catalytic reactions. Although this Perspective is mostly aimed at heterogeneous catalysis, it is important to realize that the strengths of SERS are not necessarily limited to this field of research and can also be applied to the field of homogeneous catalysis.[32,33] Furthermore, SERS is promising to become one of the tools of choice for monitoring the dynamics of biological macromolecules in biomedical applications and is useful for the characterization of biocatalysts, although its current main use is in diagnostics.[34,35]
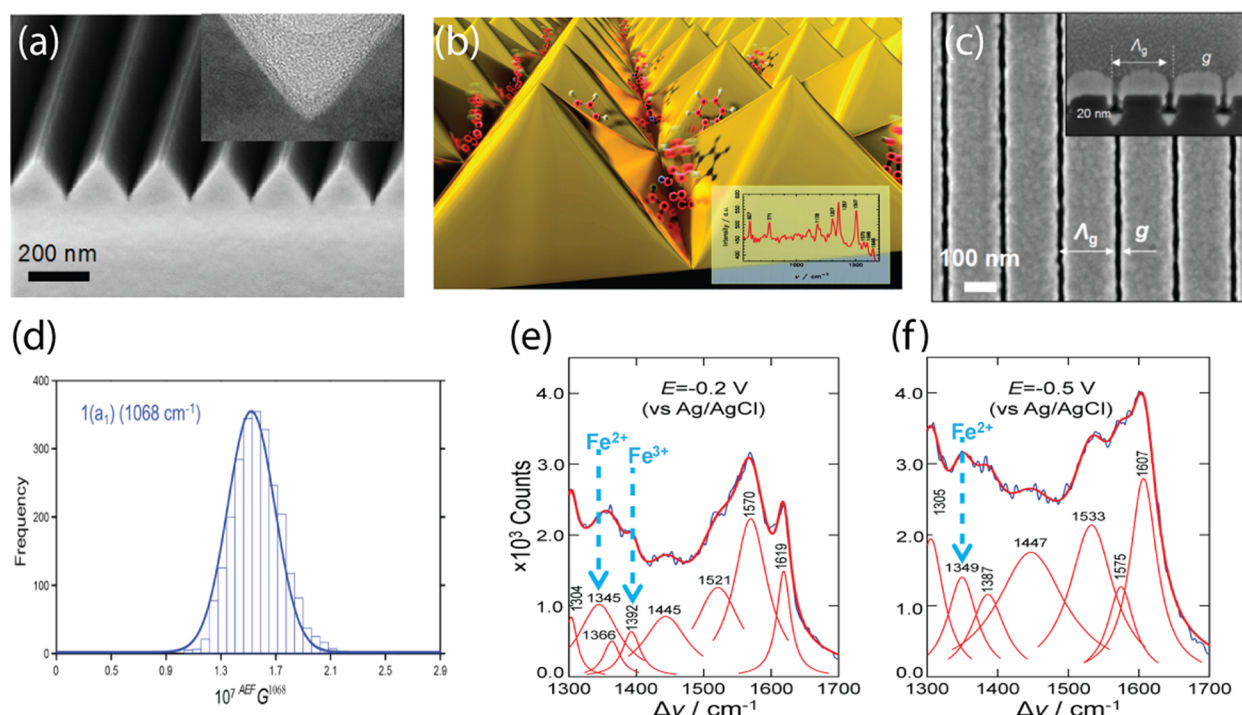
SERS. The strong Raman signal enhancement in SERS arises from the excitation of a localized surface plasmon in metallic nanostructures by an external oscillating electric field that matches the resonant frequency of the plasmon. Metallic nanoparticles are polarized by the electric field, and the induced dipole will resonate with the frequency of the incident light. This phenomenon is known as a "localized surface plasmon resonance" (LSPR) and creates a strong localized electromagnetic field, which strongly enhances the Raman signal from analyte molecules in close vicinity of the metallic nanoparticles. The strength of SERS signals dissipates by r^{-10} to r^{-12}, depending on the substrate and analyte.[17−19,36,37] This distance dependency makes the technique an ideal surface-specific characterization technique.

SERS substrates are often fabricated from gold and silver nanoparticles. Depending on their size, shape, aggregation state, and the properties of the excitation laser, the Raman signal can be enhanced by over a factor of 10^6.[17−19,31,38] Silver

nanoparticles provide stronger SERS signals than gold nanoparticles; however, gold nanoparticles are often preferred because of their higher stability.[39] Indeed, gold nanoparticles are more stable than their silver counterparts and are therefore easier to handle and store. Additionally, they are more likely to retain their SERS activity during experiments requiring elevated temperatures and/or pressures. However, because silver nanoparticles are more SERS active for laser excitation below 600 nm, they provide stronger signal enhancement since Raman scattering intensity is proportional to λ^{-4}.

The strongest signal enhancements in SERS substrates are obtained from so-called "hot spots", sites that have the strongest LSPR. For example, at the junction between a nanoparticle with another nanoparticle or a bulk metal surface, the surface plasmons can overlap to form gap-mode plasmons (Figure 1a,b). Depending on the distance between the particles, these gap-mode plasmons tremendously enhance the signal intensity in comparison to single particles, and it vanishes quickly when they move away from each other (Figure 1c−e).[40,41] This knowledge of hot spots illustrates the difficulty of applying SERS to other catalysts besides silver, gold, and copper. Since the highest enhancements come from between two plasmonic particles, one of the largest challenges becomes the observation of surface species and adsorbates on other catalytic materials.

Micro- and Nanostructured SERS Surfaces. Nanoparticle-based SERS offers advantages in terms of ease of preparation and control of chemistry, but has limited reproducibility due to surface inhomogeneity, varying dimer orientation, and ill-defined dimer spacing. For over a decade efforts have been made to create SERS surfaces with well-defined and homogeneously distributed hot spots using a variety of methods such as nanoimprinting, e-beam lithography, focused ion beam (FIB) milling, laser interference lithography (LIL), and template-based technologies that are much more promising.[42,43] Of these methods, photolithography holds great promise because of its exact geometric control and availability of an extensive technological toolbox. With this

Figure 2. (a) Nano v-grooves,[46] (b) artist's impression of nanopyramids,[46] (c) nanowires and nanogaps with cross section in inset,[45] (d) histogram of analytical enhancement factor (AEF) on a nanowire−nanogap substrate,[45] (e) −0.2 V and (f) −0.5 V spectro-electrogram of MPY/ hemin modified gold nanowire electrodes with the Fe^{2+} and Fe^{3+} bands indicated.[48] Reprinted from refs 45, 46, and 48. Copyright 2013, 2010, and 2015, respectively, American Chemical Society.

technique, structures such as nanogroove, nanopyramid, and nanogap−nanowire arrays have been recently realized with tunable gap spacing and high spatially averaged analytical enhancement factors (AEF),[44] as shown in Figure 2.[45,46] Since in the first two of these approaches LIL is used in combination with anisotropic (100) silicon etching to create nanometer pitches and spacing, no mask is needed and the method is therefore relatively cheap. However, a disadvantage of these anisotropically etched structures is that the SERS hot spots with high signal enhancement occur only at a very small percentage of the surface area because the groove width and spacing between the pyramid sidewalls vary strongly. The third structure, the nanogap−nanowire, is particularly interesting for two reasons. First, the gap size remains constant (<20 nm) as opposed to the groove and pyramid structures, while a large percentage of the surface gives high AEFs. The latter fact is due to the extremely high nanogap density of ∼1000 m·cm^{-2}.[45] In Figure 2d it is shown that practically all of the 2500 spots measured (at 1068 cm^{-1}) exhibit AEF values between 1×10^7 and 2×10^7 with an average value of 1.5×10^7.[45] The second advantage of the nanowire−nanogap structure is that it offers the opportunity of combining electrochemical reactions with in situ SERS analysis. Such a spectro-electrochemical technique gives the opportunity to study redox reactions and electron-driven processes in situ and has great importance for the study of catalytic reactions. It has also been shown to be of great value for studying and analyzing adsorbates, chemisorbed species, and reaction intermediates.[47] The nanowires can be contacted electrically in an interdigitated way under potentiostatic control, and finally the nanostructured surface can be integrated in a microfluidic system. For example, such a setup can be utilized to measure the spectral shift of iron
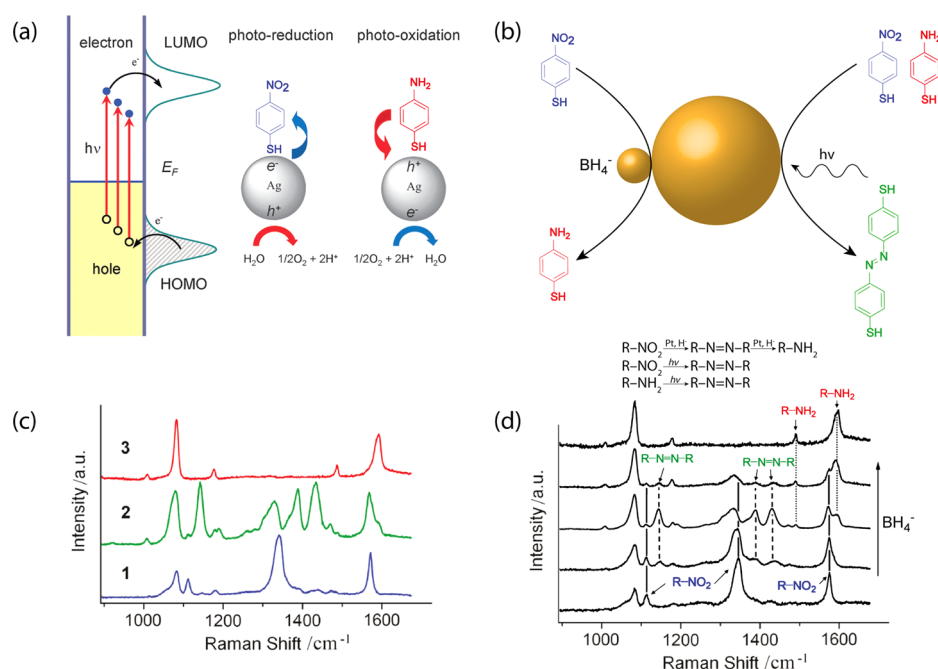
bands upon using a Ag/AgCl reference electrode and a platinum counter electrode. It was found that when the redox state of the hemin group of the mercaptopyridine (MPy)/ hemin modified gold nanowires was changed by shuttling the voltage between −0.2 V (Figure 2e) and −0.5 V (Figure 2f) versus Ag/AgCl, a corresponding change in the SERS spectra was observed.[48] This demonstrates that a combination of orthogonal analytical techniques combined with dynamic control of environmental conditions using microfluidics clearly holds great promise for in situ study of catalytic reactions.

Combining SERS and Catalysis. Gold and silver metal nanoparticles show catalytic behavior in a variety of reactions, implying that they can simultaneously act as sensor as well as catalyst.[49,50] Gold and silver catalysts can generally be used in three different types of surface reactions: heterogeneous catalysis,[51] electrochemical reactions,[47] and photocatalytic (plasmon-driven) reactions.[52−54]

Valuable industrial reactions, such as NO_x reduction,[55] epoxidation reactions,[50,56] and methanol synthesis[57] can be carried out over copper and silver metals. However, because of their lower stability in air, they are less implemented in SERS in comparison to gold nanoparticles. Alloys made from silver/gold or copper/gold often have higher stability than pure materials. Gold−silver alloys can be fabricated for example by a simple coreduction of $HAuCl_4$ and $AgNO_3$ using trisodium citrate.[58] Star-shaped copper/gold alloys have been prepared as well by a coreduction using glucose as reductant.[59] The introduction of other metals during the synthesis to prepare alloyed nanoparticles not only is interesting to increase the stability, but also will affect the position of the LSPR as well as catalytic activity.[60]

A recent study by Marimuthu et al. showed that the oxidation state of surface atoms in copper nanoparticles can

Figure 3. (a) Schematic diagram of the formation of hot electrons and holes in silver nanoparticles, which are able to catalyze both oxidative and reductive reactions.[79] (b) Possible reactions occurring during the chemical reduction of 4-NTP by NaBH$_4$ over gold nanoparticles. (c) NMF-calculated SERS spectra of the three pure components including their assignment to the three molecular species 4-NTP (blue), 4,4′-DMAB (green), and 4-ATP (red).[98] (d) Raw SERS spectra of the reduction of 4-NTP to 4-ATP over Au/Pt/Au catalysts, including DMAB-associated peaks for intermediate volumes of NaBH$_4$ added, corresponding to the calculated spectra from panel c.[98] Reprinted with permission from ref 79. Copyright 2012 Royal Society of Chemistry. Reprinted from ref 98. Copyright 2011 American Chemical Society.

be tuned by light during the epoxidation of propylene.[56] When the LSPR of the metallic core of the particles is excited, the subsequent increased electric field or hot electrons can reduce the copper oxide shell. The threshold light intensity to reduce the copper oxide surface was found to be 550 mW/cm^2, meaning that Raman lasers can easily be used to reduce the oxide surface. A plasmonic material that can reduce its oxidized surface by using Raman lasers sounds like the ideal SERS substrate. However, although the threshold intensity is far below the laser intensity used in SERS, we are skeptical whether this can be applied for SERS experiments because this mechanism has not been mentioned anywhere else in the literature.

When SERS activity and catalytic activity do not go hand in hand, innovative materials have to be applied. For example, gold nanoparticles become most catalytically active for sizes of approximately 5 nm,[61,62] whereas particles smaller than roughly 20 nm do not give a significant Raman signal enhancement.[63] Several research groups have devised methods to combine the catalytic activity of small gold nanoparticles with bigger SERS particles. By varying the synthesis conditions of a seeded growth method slightly, 125 nm gold particles were prepared with porous surfaces. These porous surfaces behaved in a similar fashion as sub-5 nm gold nanoparticles, whereas the overall particle provided the plasmonic enhancement for SERS.[64] Other methods describe the use of particles with different exposed facets,[65] adsorbing small gold nanoparticles to gelatin-covered SERS particles,[66] or by adsorption of smaller gold particles to an oxide-coated plasmonic particle.[67]

Model Reactions. One of the most investigated reactions in recent SERS studies is the reduction of 4-nitrothiophenol (4-NTP) to 4-aminothiophenol (4-ATP).[68] Thiol-functionalized

molecules, such as 4-NTP and 4-ATP, exhibit high affinity for metal surfaces, guaranteeing their close contact with the SERS substrate. Additionally, the Raman scattering cross section of molecules containing nitro- and amino-functionalized groups in combination with aromatic rings is relatively large, and at certain excitation wavelengths this can lead to resonance Raman scattering. Furthermore, the use of thiols in catalysis gives the possibility of studying the kinetics of surface reactions with only minor interference of diffusion, adsorption, and desorption mechanisms because they are fixed on the surface. The combination of these properties makes 4-ATP and 4-NTP ideal model molecules for SERS experiments.

The reduction of 4-NTP by NaBH$_4$ requires the presence of a metal catalyst and can be performed at ambient conditions. Consequently, gold and silver nanoparticles meet the requirements for both catalysis and SERS substrate. Various papers and reviews have already been published concerning the reactions of 4-ATP and 4-NTP.[54,68−73] Model studies using 4-ATP and 4-NTP molecules can be used to increase our understanding of SERS in catalysis and to gain more insight into the interpretation of SERS spectra. Herein, we present several recent examples to demonstrate the possibilities and also the difficulties of interpreting SERS results.

By preparing well-defined particles with different morphologies, it is possible to link structure of a catalyst to its performance. However, it should be kept in mind that SERS activity is strongly dependent on a particle's size and shape. Since the electric field enhancement is highly local, it is inherent that the probing area of SERS measures only a fraction of the catalytically active surface. For example, Zhang and Wang used gold nanoparticles with different geometries

to study their facet-dependent catalytic activity for the reduction of 4-ATP to 4-NTP with SERS.[65] As expected, high-index faceted particles were the most active according to the data obtained by SERS. However, the more anisotropic particles required a much shorter acquisition time for sufficient SERS signal in order to observe clear bands in the spectra, indicating that these particles exhibit intrinsic hot spots. Drawing conclusions about the overall catalytic activity of a particle is therefore difficult with SERS because the Raman signal intensity at hot spots is several orders of magnitude stronger than over the rest of the particle and therefore dominates the overall spectrum. Additional studies, such as ultraviolet−visible (UV−vis) measurements, should then be performed for comparison.

Plasmon-Driven Reactions. SERS cannot simply be used as a noninvasive characterization technique; the plasmonic nanoparticles can interfere with the reaction of interest in multiple ways.[28,52,69,74−76] First, the massive electromagnetic field near the surface can weaken certain bonds in the analyte, initiating reactions.[28] Second, the heat generated as a result of the absorbed light will change the reaction conditions, affecting both temperature[77] and subsequently analyte concentrations.[73−78] Third, the plasmonic particles can generate new and alternative reaction pathways by the formation and injection of hot electrons (Figure 3).

Hot electrons can be generated at hot spots, where electrons are excited from below the Fermi level to an occupied state below the vacuum level. When an electron-acceptor is close to the surface, these "hot electrons" can be injected into the lowest unoccupied molecular orbital (LUMO) of this molecule. Simultaneously, the hole can also accept electrons from the highest occupied molecular orbital (HOMO) of a nearby molecule (Figure 3a).[79]

The three alternative pathways can take place simultaneously and can affect each other. These side effects do not mean that SERS is useless for catalysis; however, it does mean that one has to make sure that what is measured is definitely the reaction of interest, and not a SERS artifact. Additionally, the three side effects can be advantageously used to initiate reactions, for example by extreme heating of the sample by applying pulsed lasers.

> One has to make sure that what is measured is definitely the reaction of interest and not a SERS artifact.

The use of plasmonic materials as catalysts has recently become a growing field within photocatalysis because it can produce chemicals with alternative pathways at ambient temperatures. Because both the reaction and the SERS signal are the strongest at hot spots, SERS seems to be an ideal method to study plasmon-driven reactions.[71] Photocatalysts are useful as wastewater treatment and as a sustainable energy-supplier for the future,[80] and plasmon-driven catalysis is an exciting field in its own right. Interested readers are therefore directed to the recent literature.[28,54,69,76]

To study conventional catalysts, one has to make sure that the characterization technique does not interfere with the reaction of interest. Decreasing laser energy and power and changing the polarization 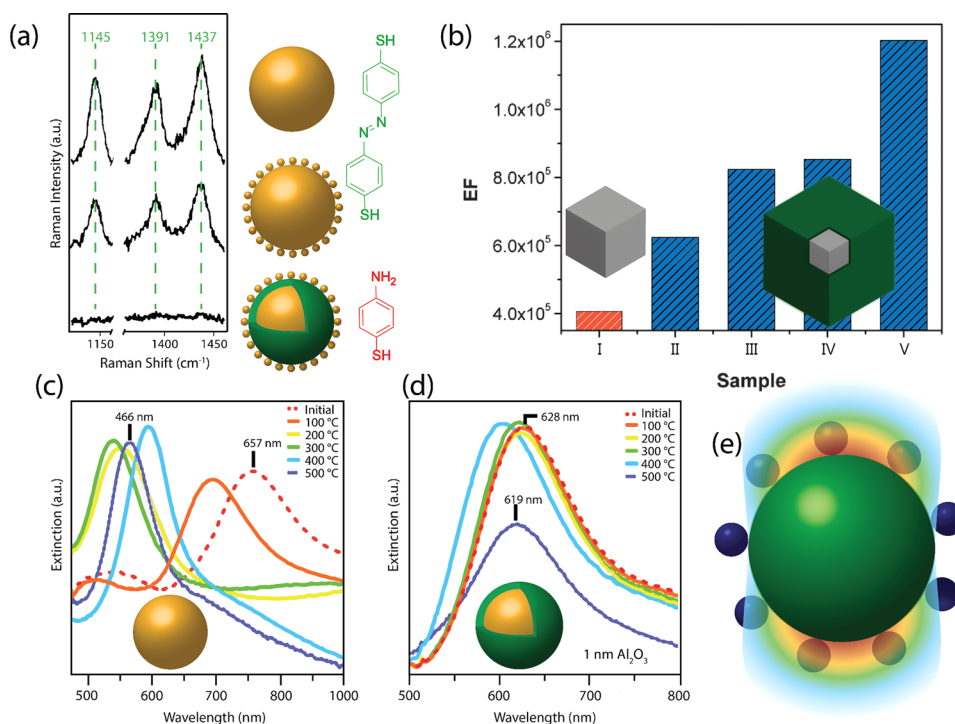are known to affect the catalytic power of the plasmons, although the signal-enhancing effects of the plasmonic particles are thereby sacrificed.[29,72,81]

Borrowing SERS Activity. Because SERS is limited to a few materials,[82−84] SERS activity has to be "borrowed" from existing substrates when the catalyst itself is not SERS active.[85] Catalytically active nanoparticles can be directly assembled on a SERS substrate. Joseph et al., for example, reported a novel method to study the reduction of 4-NTP to 4-ATP over platinum catalysts.[33] The SERS signal of 4-NTP was used to obtain kinetic data of the reaction in solution. The 2 nm platinum particles were either randomly deposited over a SERS substrate consisting of gold nanoparticles or were used in colloidal solution. Since the reaction data of immobilized particles was not significantly different from the colloidal catalyst, the reaction mechanism is thought to be the same; thus, this method of immobilizing catalyst nanoparticles can possibly be applied to other chemical reactions as well.[33] However, this method does not give information exclusive to the platinum-catalyzed reaction because the gold particles are not entirely inert nor are they isolated.

Postsynthesis mixing of separately prepared Au and Pt NPs can result in a heterogeneous distribution of different particles throughout the sample. To guarantee close contact between sensor and catalyst, thin overlayers of catalytically active metal can be sputtered over existing SERS substrates. For example, Heck et al.[86] prepared gold nanoshells with submonolayer coverages of palladium and observed improved activity for the aqueous-phase hydrodechlorination of dichloroethylene (DCE). These nanostructures allowed for the detection of the dechlorination of 1,1-DCE to ethane. Although the signal intensity of the probe molecule 4-ATP was reduced after palladium was grown on the gold nanoshells, the signal intensities of adsorbed 1,1-DCE increased, indicating the stronger interaction of 1,1-DCE to Pd. The dechlorination at the surface was observed by the appearance of peaks associated with Cl−M and C−M bonds. Additionally, a range of intermediate structures from 1,1-DCE to ethane were detected.[86]

Core−shell nanoparticles can be fabricated by colloidal synthesis as well.[85] Using this method, any direct interaction with the plasmonic particle can be prevented when a uniform coating is applied. A crucial side effect can take place when thin metal layers are deposited over other metals. Due to the formation of alloys or by electron transfer from the core to the shell, the electronic structure of the catalyst may change, influencing its activity.[87] It has been reported that it is necessary to keep the metal coatings at least 5 monolayers thick so that it behaves as a "pure" material.[88] Attard et al. have used a colloidal method to produce platinum-coated SERS particles for studying the effect of surface poisoning on the alkyne adsorption on platinum catalysts.[89]

Because SERS substrates are heterogeneous by definition, the materials will have to be cleverly designed for homogeneous catalysis depending on the desired results. To increase the signal of low concentrated catalysts, reactants, and products, the materials can be simply mixed in solution.[33] However, when these materials show a negative affinity to the SERS substrates, insufficient signal will be obtained and no conclusive spectrum can be formed. Additionally, some molecules in the solution might have a higher affinity to gold or silver (also depending on the facets), increasing the chance to observe them and simultaneously decreasing the chance to observe other molecules. Similar to heterogeneous

Figure 4. Advantages of SHINs over bare gold nanoparticles. (a) SHINs prevent plasmon-driven reactions. SERS spectra collected from 4-ATP adsorbed on 80 nm gold particles, 80 nm gold nanoparticles covered with 5 nm gold particles, and 80 nm SHINs covered with 5 nm gold particles. DMAB is not observed when SHINs are implemented.[67] Adapted from ref 67. Copyright 2013 American Chemical Society. (b) SERS EF calculated for a variety of silver nanocubes: bare (I, red) and SiO_2-coated cubes using different methods (II−V, blue). All SiO_2-coated nanocubes show increased EFs compared to bare silver nanocubes.[99] Adapted with permission from ref 99. Copyright 2015 Royal Society of Chemistry. (c) UV−vis absorption spectra of gold nanoparticles at elevated temperatures indicate that their LSPR shifts above temperatures of 100 °C.[94] (d) UV−vis absorption spectra of gold nanoparticles coated with 1 nm alumina at elevated temperatures indicate that stability is maintained up to 400 °C.[94] Adapted from ref 94. Copyright 2007 American Chemical Society. (e) SHINs (green) could potentially serve as a support for many other catalysts (purple spheres). Because the electric field is stronger (red) at the surface of the SHIN, it is expected that the catalyst−support interface can be characterized.
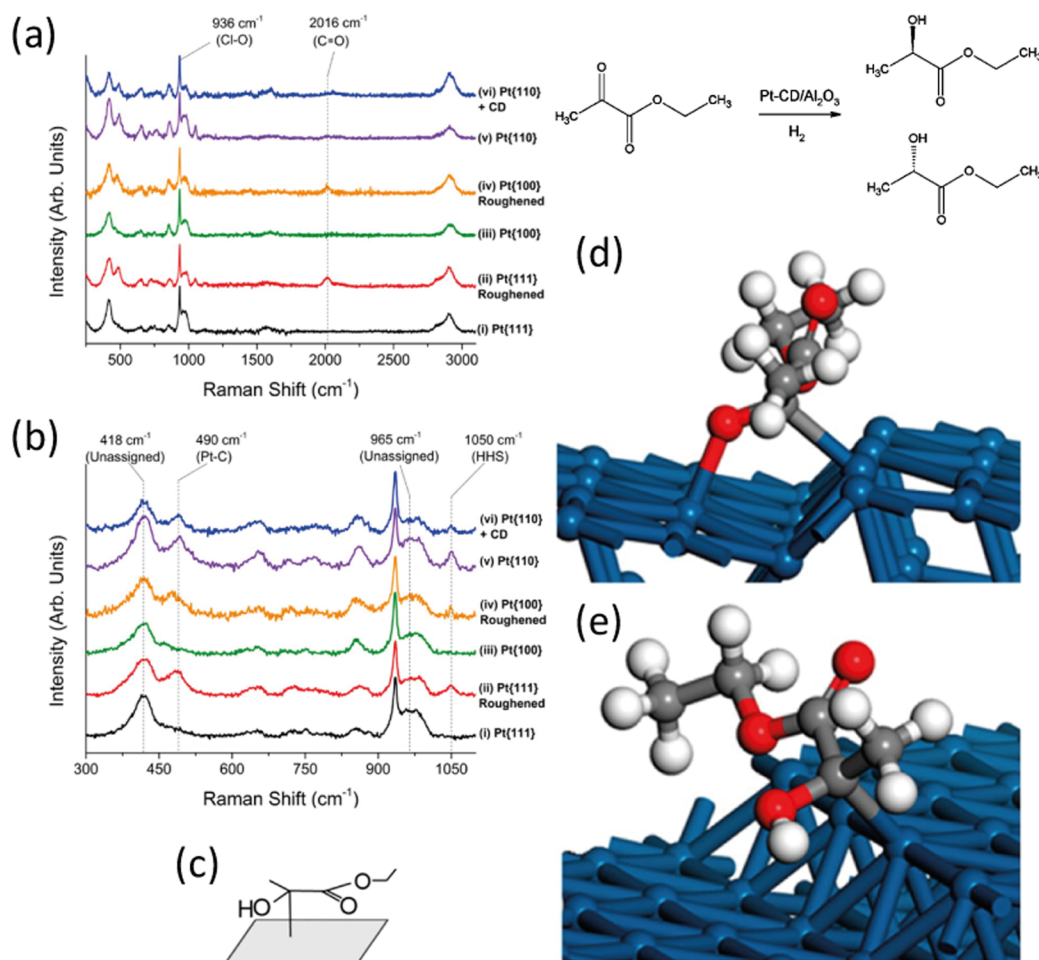
catalysis, the catalysts are preferred to be fixed to the surface of a well-defined SERS substrate so that we know what we are looking at. Other methods are to fix the catalysts to a self-assembled monolayer (SAM) on a gold substrate or to induce aggregation between the nanoparticles by introducing the catalyst.[34,35,90]

SHINERS, for Stable and Noninvasive Characterization. A promising method to minimize plasmonic side-reactions is isolating the noble metal nanoparticles using thin dielectric oxide coatings. Coatings of <10 nm thick silica have been proposed to make plasmonic particles inert.[91] The technique, quite aptly named "shell-isolated nanoparticle-enhanced Raman spectroscopy" (SHINERS), has been successfully applied, among others, to study catalysts.[67,91−93] Coating of nanoparticles with oxides enhances their stability in demanding conditions and increases their shelf life. Al_2O_3 shells of less than 1 nm thick can enhance the stability of the nanoparticles to withstand temperatures of up to 500 °C under nitrogen for a few hours (Figure 4d,e).[94] The improved stability makes SHINERS a highly promising technique to study a wide variety of heterogeneous catalysts. Shell-isolated nanoparticles (SHINs) can be used for expanding the SERS activity to other materials because the oxide coating reduces plasmon-driven reactions (Figure 4a) and increases the stability of the plasmonic particle (Figure 4c,d).

An effective method to implement SHINERS in catalysis is to prepare a physical mixture of bulk catalyst material with SHINs. Such a strategy was used by Li et al. to study nickel-

based solid oxide fuel cell (SOFC) anodes. Spherical silver nanoparticles were coated with 10 nm thick silica layers to increase their thermal stability, enabling them to withstand temperatures of up to 500 °C. However, due to the thickness of the coating the Raman signal was enhanced only by a factor of 150. Even with this low EF, the authors were able to observe surface species in ceria (CeO_2) at elevated temperatures and detect small quantities of coke that lay beneath the sensitivity limit of conventional Raman spectroscopy. Li et al. state that this technique can be readily applied to other catalytic and electrochemical systems, and we feel similarly. This method is highly suitable for the detection of surface species and adsorbates and could show even greater potential when more stable and/or thinner coatings can be produced.[92,93]

The oxide layer can furthermore serve as a support material for nanoparticles (Figure 4e), facilitating close contact between the SERS-active particle and the catalyst.[67,96,97] Similarly to other studies concerning the reduction of 4-NTP to 4-ATP,[64,65,98] Xie et al. observed DMAB as intermediate when the large plasmonic particles were not coated with silica.[67] However, when the large particle was isolated by an ultrathin (~1.5 nm) but nonporous silica coating, the bands associated with DMAB were no longer observed and only the reduction of 4-NTP to 4-ATP was detected (Figure 4a). Gold catalysts of 5 and 10 nm deposited on the silica layer were used to show that smaller particles were indeed more effective catalysts.

Figure 5. (a, b) SHINERS spectra of Pt{hkl} single crystals immersed in 0.1 M EP/0.1 M HClO₄ recorded under hydrogen evolution conditions (−0.1 V). (c) Schematic depiction of the half-hydrogenated state (HHS) intermediate. (d) Calculated structure of EP adsorbed in the μ_2(C,O) configuration. (e) Calculated structure of HHS at a Pt{221} surface. Reprinted from ref 95. Copyright 2016 American Chemical Society.

A similar approach was applied by Attard et al. where they used silica-coated gold nanoparticles on single-crystal platinum surfaces to observe adsorbates with SHINERS, and more recently during the hydrogenation of ethyl pyruvate (EP) to (R)-ethyl lactate (EL) over modified and unmodified Pt{hkl} electrodes.[89,95] SHINs deposited on different platinum surfaces proved to noninvasively enhance the signal of EP adsorbed to the surface. An intermediate structure of the ethyl pyruvate, more specifically a half-hydrogenation state (HHS), was formed by addition of a hydrogen atom to the keto carbonyl group; in addition, a new species was identified as intact chemisorbed EP bound in a μ_2(C,O) configuration, as illustrated in Figure 5 with a series of SHINERS spectra, as well as for the calculated structures of Pt-chemisorbed EP and HHS.[95] The relative ratio of both species was sensitive to the Pt surface structure. More specifically, the μ_2(C,O) EP surface species was dominant at pristine Pt{111} and Pt{100} surfaces, whereas the HHS was observed only at surfaces with defects and kinks, such as Pt{110} and roughened Pt electrodes.

In our lab, the dimerization of 4-ATP over pinhole-free SHINs was observed, contradicting the previously mentioned experiments.[70] This indicates that in the research conducted by Xie et al. the rate of plasmon-driven reactions is most likely slowed significantly by the SiO₂ coating in comparison to the reduction by NaBH₄, making the observation of DMAB impossible.[67] In many publications, side effects are reported to be caused by hot electrons injected into nearby molecules, but we believe that the extremely strong electric field facilitates photosensitive reactions as well.[28] Although SERS intensity can increase for some coated particles (Figure 4b),[99] increasing thickness of oxide coatings will result in a decrease of the signal-enhancing effect and prevent side reactions caused by hot electrons or a strong electric field.

Any catalyst can potentially be assembled on the surface of SHINs, allowing the observation of Raman active surface species on these catalysts. These particles can then be tuned in size, shape, and structure to characterize the effect on the reaction, similar to the method described by Xie et al.[67] One could also make use of different oxide[91,100,101] or carbon[102] coatings to mimic the support material, although some combinations of materials are effective photocatalysts, such as titania-coated gold nanoparticles.[74,100] A coating of several nanometers separates the catalyst particle and the plasmonic particle, meaning that for increasing catalyst size, the signal intensity decreases dramatically for the far side of the particle (Figure 4e). The strongest signals are produced at the metal–support interface in comparison to the far side of the particle. This effect can be exploited by attaching larger catalysts to the surface, making it more likely to observe reactions or catalyst structures at the support–catalyst interface.[103]

Tip-Enhanced Raman Spectroscopy. To directly relate catalytic activity with the morphology of catalysts, we need to map and monitor catalytic activity on a single catalytic particle. Instruments with high sensitivity and above all nanoscale spatial resolution are required to reach this goal.[104] Therefore, a more direct method to correlate catalyst structure to activity is by combining high chemical sensitivity of SERS with nanoscale spatial resolution of scanning probe microscopy. To showcase the possibilities of the AFM−Raman methodology, the catalytic activity of silver nanocubes in rhodamine 6G degradation was linked to their distribution.[105] However, the diffraction-limited spatial resolution of Raman spectroscopy (typically 200−300 nm) is not overcome by combining SERS and AFM.
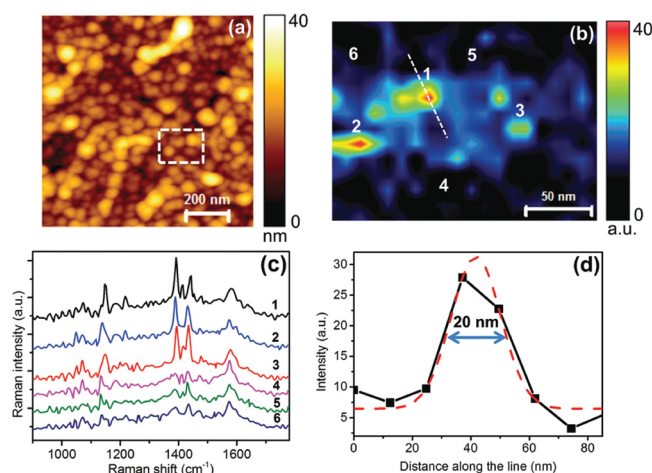
The spatial resolution can be significantly improved when a metal-coated tip is implemented; this technique is referred to as TERS.[106] Compared to SERS where hot spots are randomly distributed over the substrate, the electromagnetic enhancement in TERS occurs only at a single point of the TERS tip-apex, which can be scanned over a surface using sensitive SPM feedback to make a nanoscale map of surface chemistry and catalytic activity simultaneously with the topography. TERS improves the diffraction-limited spatial resolution of confocal Raman spectroscopy to the nanoscale, with a recent breakthrough reaching the subnanometer regime with STM-based TERS demonstrating the capability of TERS to map even single molecules.[27]

The potential of TERS for in situ catalysis research was first demonstrated by Domke and Pettinger[107] who studied the organometallic catalyst cobalt *meso*-tetraphenylporphyrin (CoTPP) on Au(111) substrate using STM-TERS with a Au tip. With TERS, the authors could spectroscopically discriminate between axially complexed and ligand-free CoTPP regions on the Ag substrate and identify chemical species complexed with CoTPP. TERS spectra from well-ordered CoTPP regions identified in the STM topography images showed vibrational bands characteristic of linker-modified CoTPP sandwiched between two Au layers, whereas TERS spectra from the disordered region showed vibrational features of CoTPP axially complexed with CO and NO formed by catalytic reduction of CO_2 and NO_2 from ambient air. This study demonstrates that TERS can be successfully used to correlate structure with catalytic activity in heterogeneous catalysis, while the observation of such complexes indicates possible applications in homogeneous catalysis.

Studying Light-Triggered Reactions with TERS. TERS studies of the plasmon-driven photocatalytic reaction (4-NTP to DMAB) was carried out for the first time in a collaborative effort by Weckhuysen and Deckert et al.[29] The reaction was triggered using a 532 nm laser and was unobtrusively monitored using a 633 nm laser. It was found that a complete self-assembled monolayer (SAM) is necessary to obtain a stable starting signal as the molecules in an incomplete monolayer can change their orientation or move in and out of the sampling area more easily.[29] Because TERS measures only a small number of molecules and spectra are not averaged over an ensemble, signal intensities are highly influenced by small fluctuations of analyte molecules in the measured area.[108] Time-series Raman spectra measured before and after the reaction at the tip-apex clearly showed the Raman bands associated with 4-NTP decrease and DMAB increase in intensity over time. This demonstrates the

potential of TERS to monitor reactions on single catalytic particles over time.[29] Almost simultaneously, Zhang, Xu, and co-workers[109] performed a similar experiment using high-vacuum (HV) STM-TERS to demonstrate that this photocatalytic reaction is driven by hot electrons produced during surface plasmon resonance. The authors showed that the reaction can be controlled by plasmon intensity, which depends on laser power or the tip−substrate distance. In an additional report it was shown using HV STM-TERS that the reaction was indeed the result of the plasmon resonance in the nanogap between a Au tip and a Ag substrate and any thermal effects could be neglected.[110]

Very recently, the potential of TERS to actually relate catalyst structure to activity was realized by Kumar et al. with AFM-based TERS.[111] The activity of silver nanoparticles was studied using the plasmon-driven photocatalytic dimerization of 4-ATP to DMAB. The authors first mapped the reaction at a single point of contact of the Ag-coated TERS tip with a reactant substrate. Since both the silver particles and the silver-coated tip were catalytically active in the reaction 4-ATP to DMAB, the tip was made inert by applying a 3−5 nm thick Al_2O_3 coating while preserving its plasmonic enhancement. Using such an alumina-protected TERS tip, the authors were able to map catalytically active sites on the Ag substrate with 20 nm spatial resolution, as shown in Figure 6.[111]

Figure 6. (a) AFM topography image of the Ag catalyst substrate. (b) TERS map of the area marked by the dashed rectangle in panel a showing signal intensities of a DMAB-associated band at 1142 cm^{-1}. (c) Near-field spectra measured at the positions marked in panel b. (d) Intensity profile along the dotted line marked in panel b showing the spatial resolution of the TERS map using a fitted Gaussian curve (red) to be 20 nm.[111] Reprinted with permission from ref 111. Copyright 2015 Royal Society of Chemistry.

We believe that dielectric coating of TERS tips is a good strategy for obtaining reliable and stable data during measurements, similarly to the application of SHINERS. It is known that the tips can be contaminated by surface species, causing additional bands in the spectrum or worse, the loss of their signal-enhancing properties.[112] Dielectric coatings such as oxides can prevent adsorption of contaminants or irreversible tip damage from oxidative reactions, thereby enhancing their stability. However, because the decay length of TERS near-field is only a few nanometers,[113] a thick dielectric coating may significantly decrease the plasmonic enhancement of the TERS tip.[37] Therefore, the thickness of

the protective dielectric coating should not be more than a few nanometers (ideally 1−2 nm) and should be pinhole-free for TERS tips to provide Raman signal enhancements. Alternatively, aluminum-coated tips have been used in TERS in combination with a 363.8 nm ultraviolet laser.[114] Because aluminum is known to form a thin native oxide layer of approximately 3 nm, such tips are expected to be chemically more stable, although higher-energy lasers are required that may cause degradation of chemical species.[82]

The sensitivity of TERS measurements can be significantly enhanced by utilizing the plasmonic coupling of a metal or metal-coated tip with a metal substrate. Using this so-called "gap-mode" TERS, extremely high EFs can be reached. For example, gold-coated tips close to metallic substrates can produce Raman signals that are a factor of 10^3 stronger than those of tips close to dielectric substrates, such as SiO_2.[115] However, care must be taken to ensure that the metal used for the tip or substrate is not catalytically active for the reaction under study. So far, TERS has been mainly used for the study of plasmon-driven photocatalytic reactions in which the reactants and products have a rather large Raman cross section. However, the reactants and products employed in more industrially relevant catalytic reactions usually have a much lower Raman cross section. Furthermore, such reactions are carried out at temperatures and pressures much higher than ambient conditions. Therefore, TERS probes with high plasmonic enhancement, stability, and lifetime are required to make TERS a powerful tool for the study of catalytic reactions under operating conditions.

Toward the Observation of Single Molecules. Spectral fluctuations that arise in TERS and SERS experiments do not have to be an undesired result but can be a topic of interest as well. Shifts in the band position can give clues to the mechanism of a reaction. Not only do orientational effects become more visible when homogeneous broadening is reduced by measuring smaller ensembles, but also other interesting events can be observed as well. For example, one can distinguish between isotopes because vibrational energy levels are related to the reduced mass of the participating atoms.[116]

Isotopes can be useful for the study of catalytic reactions and have been implemented to reveal a variety of reaction mechanisms using techniques such as steady-state isotopic transient kinetic analysis (SSITKA).[117] However, this technique observes only the product and is not able to detect the surface species and adsorbates. Combining SERS with SSITKA could enable the characterization of surface species and possibly track the changes in the spectrum of the adsorbed molecules when it reacts with the isotopes. We believe this can provide crucial information about the specific reaction mechanisms.
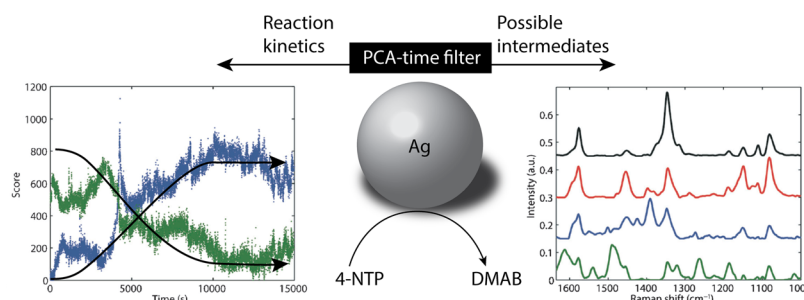
> Time-resolved Raman spectroscopy should be combined with TERS to give a spatial resolution in the nanometer scale and a temporal resolution in the picosecond scale.

Additionally, the chance to find short-lived species such as intermediates should increase when approaching single-molecule experiments. Knowing which and how many intermediates are present during the reaction is crucial to optimally tune the catalyst as it will tell us the amount of rate-limiting steps and how to possibly improve the reaction kinetics. Combining single-particle and single-molecule kinetic studies have been performed in fluorescence microscopy experiments, revealing intermediates and interparticle heterogeneities such as size-dependent activity.[118] However, fluorescence microscopy experiments do not enable the observation of structures of the reactants and requires the use of fluorescent reactants or products, thereby limiting its use. SERS, on the other hand, can supply us with structural information on both the reactant and catalyst and can be applied to a wider range of molecules, allowing a larger versatility.

To approach single-molecule experiments, the analytes can be diluted. However, dilution of the reactants cannot always be applied to obtain reaction mechanisms. Reaction conditions will often change upon dilution, and this can lead to different reaction pathways. For example, the dimerization of 4-NTP cannot proceed for single molecules, and it was expected that the reaction would therefore be inhibited. Zhang et al. found that a plasmon-driven reaction of highly diluted 4-NTP still takes place, although the diazo-product is not formed.[75] When there is no second molecule nearby, the nitro-group is split from the substrate and thiophene (TP) is obtained as the product. Hot electrons generated at the hot spots were proposed to have sufficient energy to excite 4-NTP to a transient negative ion. The negative ion "travels" to the excited state of TP and returns to the ground state of TP, returning the electron to the gold surface.[75]

Single or several molecules at hot spots can dominate the spectrum over larger ensembles because the electric field is significantly stronger than for molecules positioned at other structures. If a reaction takes place while the molecule is situated at the hot spot, we should be able to observe the reaction. Plasmonic catalysts therefore prove to be an ideal substrate for SERS experiments, because both the high signal enhancement and catalytic activity originate from the hot spot.[28,54] Previous research performed in our group utilized this principle to study the dimerization of 4-NTP to DMAB.[29,30,119] Chemometric methods were applied to obtain a clearer image of the kinetics during the reaction, demonstrated in Figure 7.[30] First, a one-component principal-component analysis (PCA) removed the spectral blinking from the data and already resulted in a lower signal-to-noise ratio (Figure 7 left panel vs middle panel). After removal of the spectral blinking, the reaction spectra were taken through a two-component multivariate curve resolution (MCR) that described the reactant and the product. This resulted in a better understanding of the reaction data with a lower signal-to-noise ratio. The spectra that were removed from the kinetic data were subsequently analyzed with a four-component MCR analysis (Figure 7, right side). Two of the components were similar to the two main components in the kinetic data, apart from some slight variations in peak intensities that were caused by differences in orientation. The third and fourth components were low in intensity over the measured time, apart from two single instances for each component. The third component resembled much of DMAB, but the fourth component is a completely unknown structure and is a potential reaction intermediate.[30]

Figure 7. PCA used to obtain kinetic data with reduced noise in SERS experiments. (Left) The conventional method to obtain kinetic data is to plot a peak area over time. (Middle) Spectral fluctuations can be removed from the spectrum with a PCA time filter, after which a two-component MCR can further clear up the kinetic data. The kinetic data is now analyzed over full spectra instead of over single peaks, making it less prone to shifts in band positions. (Right) The discarded data after the PCA time filter can be analyzed with MCR to find possible intermediate structures.[30] Adapted with permission from ref 30. Copyright 2015 Wiley-VCH.

Ultrafast Raman Spectroscopy, Watching a Molecule Breathe. Most Raman spectrometers require spectral integration times of at least a second and are therefore not fit to observe short-lived species such as intermediates. Recent progress made in the field of ultrafast Raman spectroscopy allows acquisition times in the order of picoseconds with Raman line widths of tens of reciprocal centimeters.[31] Such fast acquisition times enable the elucidation of a great deal of reaction steps and dynamics, such as bond forming and breaking. To extend the potential of time-resolved Raman spectroscopy, it can be combined with other techniques such as CARS, to improve the signal intensity, and SERS, to increase the signal intensity even further to detect surface species.[120,121]
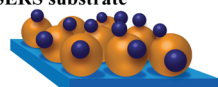
Because the technique generates extremely large electric fields that can potentially damage the sample and the SERS antennae, the experiments need to be performed in a highly controlled environment. Yampolsky et al. managed to reduce the damage to SERS-antennae by encapsulating gold dimers and adsorbed trans-1,2-bis(4-pyridyl) ethylene (BPE) in a thick porous silica shell of about 70−80 nm.[120] The hot spots

between the dimer in combination with CARS provided excellent signal enhancement for the observation of BPE near the single-molecule level. By applying a femtosecond laser scanning CARS microscope and by tuning the frequencies of the pump and the Stokes pulses, the authors were able to observe an oscillating signal that was associated with the quantum beating of the closely spaced excited vibrational modes of BPE. It is important to note that a single time trace

> The heat developed by the plasmonic materials upon illumination provides new opportunities to locally create the proper experimental conditions to trigger a catalytic reaction.

was not obtained instantly, but the result was obtained after averaging the signal over an hour.[120]

Table 1. Overview of Different SERS Substrates Including Their Advantages and Disadvantages

SERS substrate	Advantages	Disadvantages
Gold/silver/copper catalyst	Combined SERS antenna and catalyst Correlate structure to performance Simple synthesis	Plasmon-driven (side-)reactions Hot spots enhance highly locally and not over entire catalyst Low stability
Catalyst particles distributed over existing SERS substrate	Borrow SERS activity Correlate structure to performance	Gold-reactant interactions Plasmon-driven (side-)reactions Inhomogeneous distribution of particles Low stability
Core-shell particles	Borrow SERS activity Isolated gold particles	Plasmon-driven (side-)reactions Low stability Possibly altered catalyst properties
SHINs	Isolated gold particles Increased stability Can act as support material	Often decreased EFs
TERS	Able to map catalytic activity on the nanoscale Simultaneous topography and chemical information possible Structure-performance correlation	Time consuming Requires metallic substrates for higher EFs Low probe stability, can be improved with dielectric coating

Ultrafast Raman spectroscopy can lead to promising results where one could actually follow bond formation and breaking. However, the technique suffers from the possibility of sample damage and requires highly controlled environments and thus does not seem fit for the characterization of catalysts in their operating conditions yet. Ultimately, time-resolved Raman spectroscopy should be combined with TERS to give a spatial resolution in the nanometer scale and a temporal resolution in the picosecond scale. However, such experiments have to be performed on fixed analytes under ultrahigh vacuum to prevent signal blinking and signal degradation.

Challenges and Future Prospects. Based on the above considerations it should be clear that SERS and TERS can make the difference in three specific fields. The first field concerns the monitoring of chemical reactions at the molecular level, including the potential to identify reaction intermediates and even transition states. Second, the use of SERS in combination with its plasmonic platform opens up ample opportunities to conduct a wealth of chemical reactions at the surface of gold and silver, which are known to be catalytically active. The third field is associated with the heat developed by the plasmonic materials upon illumination providing new opportunities to locally create the proper experimental conditions to trigger a catalytic reaction.

It is important to realize that SERS and TERS have made tremendous progress over recent years and are becoming mature spectroscopic techniques. Improvements in substrate preparation have made SERS more robust and sensitive, opening the path for the detection of surface species with low Raman scattering cross sections in a wide range of reaction conditions. We believe that, following the highlighted examples in this perspective article, SERS can become an attractive and versatile characterization method for a wide variety of catalytic materials. However, this will not be a simple task and requires highly interdisciplinary research for developing stable and inert SERS substrates, without losing plasmonic enhancement. Simple spherical plasmonic nano-particles often do not suffice for heterogeneous catalysis research because their enhancement signal is negligible when they are not in an aggregated state.[122] Dimers or other structures, such as nanorods, are expected to give better results with respect to signal enhancement, but they are currently less stable. It is believed that SERS substrates prepared by photolithography can yield more robust and homogeneous signal intensities. Similarly, TERS tips, especially with Ag-coating, are known to degrade at a fast rate and require development of robust methods of thin, pinhole free protective dielectric coatings for prolonged measurements in ambient and especially at operating conditions of catalysts.

Creating stronger LSPRs will result in more intense Raman signal intensities but can also lead to undesired effects, such as substrate damage and unwanted side-reactions. More research effort is needed to study the role of the strong localized electromagnetic field and local heating and if ultrathin oxide layers are really able to prevent plasmonic side-reactions.

We believe that SHINERS and its TERS counterpart can play significant roles in the study of heterogeneous catalysis. SHINs have been proven to be more inert and stable than bare particles and can even act as a support material, guaranteeing close contact between catalyst and sensor for heterogeneous catalysis (Table 1). Additionally, alumina-protected TERS tips have proven to be a useful, stable, and

noninvasive technique for mapping catalytic activity of silver photocatalysts. Combining the current developments in SERS and TERS with other developments in Raman, such as CARS and ultrafast spectroscopy, will most likely lead to useful mechanistic information regarding catalytic solids.

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Notes
The authors declare no competing financial interest.

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Caterina S. Wondergem obtained her M.Sc. degree in Nanomateri-als: Chemistry and Physics from Utrecht University. She graduated cum laude in 2014 with a thesis entitled "The Effect of Water on Methanol-to-Olefins Reactions Studied by Advanced In-situ Micro-spectroscopy". Later that year she started her Ph.D. research "Unravelling the Mysteries of Solar Steam Nanobubbles" under the supervision of Prof. Bert Weckhuysen.

Naresh Kumar obtained his B.Tech. from the Indian Institute of Technology Delhi. He received his Master Degree in Physics from King's College London, where he worked on the nanoscale chemical imaging of polymer-blend thin films using TERS. Naresh has now set up an AFM-TERS system and has applied it to solve various problems at National Physical Laboratory. He started his Ph.D. research in 2015 under the supervision of Prof. Bert Weckhuysen.

Albert van den Berg was appointed as full professor on Miniaturized Systems for (Bio)Chemical Analysis at the University of Twente in 2000. His current research interests focus on microanalysis systems and nanosensors; nanofluidics; and single cells, tissues, and organs on chips, especially with applications in personalized health care, drug development, and development of sustainable (nano-)technologies.

Bert M. Weckhuysen has been a full professor in Inorganic Chemistry and Catalysis at Utrecht University since 2000. His research interests are in the development of spectroscopy and microscopy techniques for elucidating the working and deactivation principles of catalytic solids, mostly applied under true reaction conditions.

■ ACKNOWLEDGMENTS

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(44) The magnitude of the SERS enhancement is often described by the term "enhancement factor" (EF). It is a theoretical number that can be calculated with multiple methods. Each gives certain advantages over the others. Two examples of the methods to

calculate EFs are the substrate EF (EF) and the analytical AEF (AEF), which are calculated as

$$EF = \frac{I_{SERS}/N_{Sur}}{I_{RS}/N_{Vol}}$$

where I_{SERS} is the intensity of the signal under SERS conditions, N_{sur} the amount of molecules adsorbed on the substrates surface in the spot size of the incident laser, I_{RS} the average intensity of the signal during normal Raman spectroscopy, and N_{vol} the average number of molecules in the volume probed by normal Raman spectroscopy.

$$AEF = \frac{I_{SERS}/c_{SERS}}{I_{RS}/c_{RS}}$$

where c_{SERS} is the concentration of analyte under SERS conditions. For details, we refer to the pioneering work of Felidj and co-workers:

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