

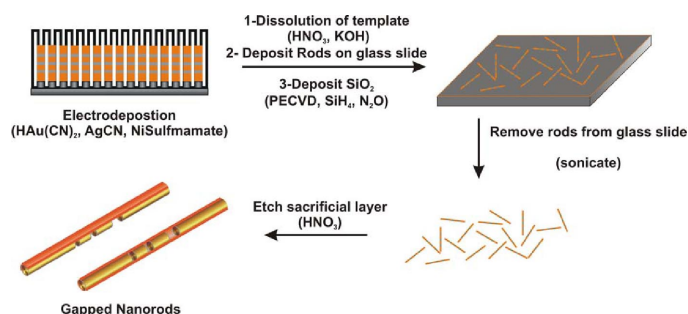
# Designing nanostructures with optimized surface-enhanced Raman scattering behavior

Matthew J. Banholzer, Jill E. Millstone, Lidong Qin, and Chad A. Mirkin

*On-wire lithography is a new nanofabrication technique that can be used to design functionalized nanowires for both encoding and biosensing applications.*

Investigations in the burgeoning field of nanophotonics have demonstrated that certain nanostructures act in previously unanticipated ways. One such behavior is surface-enhanced Raman scattering (SERS), an area of substantial interest, as demonstrated by the hundreds of scientific papers published on the subject during the past 5 years. SERS was discovered over 3 decades ago.<sup>1-3</sup> It transforms the basic Raman technique (a measure of the structure and properties of molecules based on their interaction with light that normally has very weak intensity relative to other spectroscopies) into one that has highly sensitive detection capabilities. Whereas Raman scattering is useful for analyzing the structure of small molecules and for addressing traditional analytical issues such as a material's composition in bulk, SERS promises advances in ultrasensitive detection of a variety of molecule classes. The most important among these are biomolecules such as DNA, RNA, and proteins. Such detection capabilities (which can approach single-molecule limits) could lead to very sensitive and even mobile medical diagnostic assays. Yet the SERS phenomenon is still perplexing to scientists.

The enhanced effect is most commonly attributed to electromagnetic or chemical mechanisms.<sup>4-6</sup> The latter involves charge transfer excitation between analyte molecules (i.e., molecules of interest) and the metal particles that they coat in nanostructures such as nanowires. (The closer an analyte is to the SERS-enhancing metal nanostructure, the stronger the SERS effect, hence the coating. Coating is used for detection beyond SERS as well.) The electromagnetic mechanism is dominated by plasmon excitation, leading to 'hot spots' of Raman signals around nano-sized metal particles. In SERS, these signals are highly ampli-



**Figure 1.** The OWL process.<sup>7</sup> HNO<sub>3</sub>: Nitric acid. KOH: Potassium hydroxide. SiO<sub>2</sub>: Silicon dioxide. PECVD: Plasma-enhanced chemical vapor deposition. SiH<sub>4</sub>: Silane. N<sub>2</sub>O: Nitrous oxide. HAu(CN)<sub>2</sub>: Auricyanic acid. AgCN: Silver cyanide. Ni: Nickel.

fied, generating a signal orders of magnitude more intense than a nonenhanced Raman signal. Together with the unique molecular fingerprints provided by Raman spectra, SERS signals constitute an extraordinarily powerful detection and spectroscopic modality that few other techniques can match in terms of sensitivity and data density. However, optimizing and harnessing this phenomenon have proven difficult, due in part to nanostructure morphology, which significantly affects optical properties. The fabrication of nanoparticles with controllable structures is therefore extremely important for understanding and exploiting SERS fully.<sup>7</sup>

Our group recently developed a process called on-wire lithography (OWL) that allows fabrication of 1D nanowires with nanoscale gaps along the long axis of the wire (see Figure 1).<sup>8</sup> The process starts with the synthesis of a segmented nanorod, consisting, for example, of alternating gold and nickel segments electrochemically grown on a template such as anodized aluminum oxide, which contains cylindrical pores. Some segments (e.g., nickel) are deliberately used as sacrificial layers that can

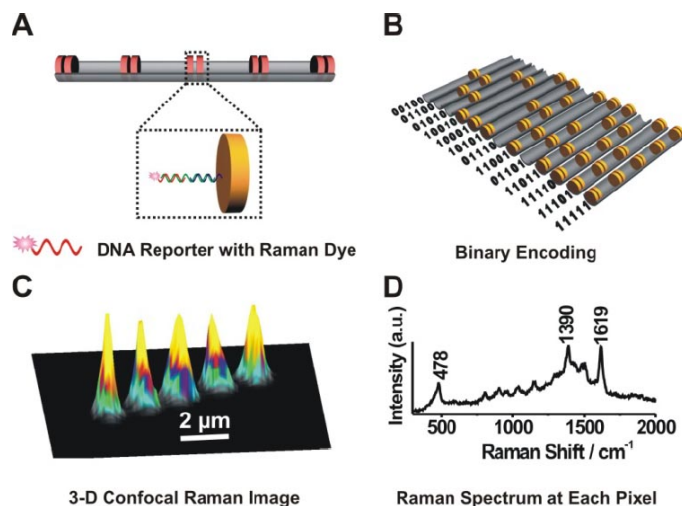
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be etched selectively to produce the desired nanoscale gaps. After nanowire growth and removal of the template, the wires are dispersed on a glass slide and coated on one face with a material such as gold or silicon dioxide. The rods are then lifted off the slide, and the sacrificial etched segments are chemically dissolved, yielding nanowires with predefined gaps and disks. OWL provides outstanding tailorability and resolution, and can be used to generate features ranging from 1nm to several microns.

The versatility of the process has allowed us to probe the relationship between feature size, gap size (down to 2nm), and Raman enhancement properties to the point of enabling the identification of the most effective SERS-enhancing structure for a given class of OWL-generated materials.<sup>5</sup> Nanodisk arrays made using the process are particularly useful for preparing SERS-active nanostructures because multiple features can be synthesized within a single nanowire. Once functionalized with a SERS-active molecule, these features can be individually probed for SERS response within the context of a single experiment. By site-isolating disk pairs along the nanorod, we can use confocal Raman microscopy to independently address each disk pair, observe individual Raman responses, and translate this data into a template for engineering the most effective SERS substrates possible, as shown in Figure 2(A).

Building on this work, we designed a novel encoding scheme based on Raman hot spots, where the presence or absence of a disk pair and associated hot spot represents either a '1' or a '0' for a binary encoding format, as illustrated in Figure 2(B).<sup>9</sup> Once functionalized with appropriate chromophores, these nanodisk codes (NDCs) are easily identified by Raman spectroscopy exploiting the SERS phenomenon, as shown in Figure 2(C) and (D). In principle, a myriad of nanodisk codes can be generated simply by varying the number and location of the pairs as well as the type and number of chromophores used as spectroscopic labels. These NDCs have the inherent ability to employ molecular labeling and physical architecture in redundant (where the dye label reporter serves to confirm the binary encoding data), collective (where both the label and the architecture give complementary encoding information), or independent (where only the label or binary structure is used) methodologies.

We recently demonstrated this possibility by using these structures in a multiplexed DNA detection assay with a 100fM detection limit: quite low for a first-generation, proof-of-concept system.<sup>9</sup> Further work could be directed toward expanding our approach to more enhancing, but harder to work with, systems made of silver instead of gold. We may also expand OWL to combine SERS-optimized structures into microfluidic systems for lab-on-a-chip applications. This would also allow us to com-



**Figure 2.** (A) Cartoon of a nanodisk code structure with DNA Raman conjugate. (B) Example of binary nanodisk encoding. (C) 3D confocal Raman microscopy image of a nanodisk code structure. (D) Representative Raman spectrum of the chromophore.<sup>9</sup> DNA: Deoxyribonucleic acid.

bine the SERS-enhancing structures with an electronic device that could actively trap analyte molecules in the SERS-enhancing locations. The development of this technology would be particularly useful to meet the rising demand for mobile detection assays and covert encoding systems. SERS can also be envisioned as a technique that will allow for unparalleled capabilities in spectroscopy and for the development of a wide variety of other detection systems.

To summarize, OWL represents a significant innovation for the fabrication of nanostructures. It can be used to probe the fundamental properties of SERS-active substrates and develop important new technologies, such as NDCs for covert encoding and biosensing applications. It represents an excellent example of how the study of nanoscale phenomena can lead to new scientific insight and technological advances.

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