Enhancing optical biosensing with aperiodicity

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Aperiodic arrays of nanoparticles provide novel opportunities to manipulate and enhance light-matter interaction.

Optical biosensing devices and functional platforms to rapidly detect and identify a wide spectrum of molecules and biochemicals have uses related to environmental monitoring, food quality control, detecting explosives, and preventing biochemical threats. Current optical biosensing technology relies on enhancing light-scattering phenomena and manipulating optical resonances on the nanoscale. These goals can be achieved by engineering electronic oscillations in metallic nanostructures, known as localized surface plasmons (LSPs). When LSPs are resonantly excited, the intensity of the incident electromagnetic fields is enhanced over nanoscale spatial regions, creating ‘electromagnetic hot spots’ that are the basis of numerous optical sensors.

Tailoring plasmon resonances by engineering nanoparticle size/morphology and array structures provides unprecedented opportunities for sensing applications. In particular, multiscale nanoparticle arrays (with interparticle separations that fluctuate from nanoscale distances to scales comparable to the wavelength of light) support a large number of photonic-plasmonic coupled resonances, which significantly boost the intensity of localized electromagnetic fields. A simple example of ‘array driven’ photonic-plasmonic coupling, also known as Fano-type coupling, is provided by metal nanoparticle gratings. Periodic gratings support a discrete spectrum of photonic resonances (i.e., diffractive or grating modes) that can strongly couple, under appropriate excitation wavelengths and incidence angles, to LSP modes of individual nanoparticles, leading to larger values of electric field enhancement and optical cross sections.

At the other extreme of structural complexity, roughened metal surfaces and random media have demonstrated dramatic enhancement of the linear and non-linear optical properties of semiconductor quantum dots and single molecules. However, the technological appeal of disorder-induced resonances, such as the celebrated Anderson localized modes in random dielectrics, is still very limited. Random structures, while providing a convenient path to electromagnetic localization and enhancement, lack simple predictive models and engineering design rules for deterministic optimization. These difficulties strongly limit the ability to conceive, manipulate, and engineer optical resonances and scattering phenomena in nanoparticle systems without spatial periodicity.

We have focused on the computational design, nanofabrication, and engineering applications of multi-scale nanoparticle arrays with a degree of structural complexity that interpolates in a tunable fashion between disordered random systems and regular periodic structures. We refer to this general class of metal-dielectric metamaterials as deterministic aperiodic nanostructures (DANS). Unlike disordered random systems, DANS are generated by deterministic algorithms rooted in discrete geometry, symbolic dynamics, and number theory. Deterministic aperiodic arrays of metal nanoparticles (i.e., plasmonic DANS) often manifest unique light localization and scattering properties, can be fabricated using conventional nano-lithographic and imprint techniques, and are amenable to predictive theories. Figure 1 shows scanning electron micrographs (SEMs) of three representative plasmonic DANS composed of gold (Au) nanoparticles and fabricated by EBL. By combining light scattering...
spectroscopy with rigorous electrodynamics calculations, we have shown that plasmonic DANS offer superior engineering control over the spatial, angular, and spectral distribution of localized optical modes. We have developed novel sensing concepts and modalities that are uniquely enabled by the manipulation of spatial frequencies in aperiodic Fourier space.

In contrast to traditional photonic gratings or photonic crystal sensors, which resonantly trap light within small volumes, DANS sensors support denser spectra of optical resonances, known as ‘critical modes,’ which display characteristic spatial fluctuations, localization, and transport properties. In the context of optical biosensing, we have shown that engineering critical resonances gives rise to efficient photon trapping effects that enhance light-matter interactions on planar substrates and boost sensitivity to surface refractive index variations. We have also discovered that light scattering by DANS substrates with various incommensurate length scales produces characteristic ‘colorimetric fingerprints’ that are easily detected using white light dark-field microscopy (see Figure 2). These complex chromatic patterns of scattered radiation provide exciting opportunities for multiplexed colorimetric detection where both spatial and spectral information are simultaneously used.

Based on this concept, we recently showed that nanostructured aperiodic surfaces, in combination with image autocorrelation analysis of scattered radiation, are ideally suited for colorimetric biodetection with visible light, defining a novel optical sensing approach with large dynamic range, sensitivity, and multiplexing capabilities. In particular, we demonstrated plasmonic DANS elements with sensitivity to protein monolayers and experimentally proved their ability to detect, with visible light, protein layers a few tens of angstroms thick. Very recently, we successfully integrated aperiodic arrays of gold nanoparticles and polydimethylsiloxane microfluidic devices using EBL and soft lithographic imprinting techniques, paving the way to multiplexed and optofluidic lab-on-a-chip platforms for spatial-spectral biochemical detection. In addition, we have shown that plasmonic DANS with aperiodic Vogel spiral order enable novel optical control, such as the ability to manipulate orbital angular momentum and to enhance broadband optical nonlinearities on a chip. Vogel spirals are deterministic aperiodic systems that lack both translational and rotational symmetry and display distinctive optical properties in between amorphous and random systems. We have also obtained isotropic structural coloration of metal surfaces by engineering hyperuniform plasmonic DANS structures.

We have also shown that plasmonic DANS are ideally suited to enhance the local intensity of electromagnetic fields over predefined nanoscale regions with broad frequency spectra. These are key attributes for engineering label-free biosensors based on the fingerprinting surface-enhanced Raman scattering (SERS) effect. SERS spectroscopy is a well-established and highly sensitive technique for investigating the specific vibrational modes of a variety of different analytes. In particular, SERS has been successfully applied to label-free chemical and biological sensing. In addition, it has great promise for rapid identification of viruses and bacteria, potentially enabling whole-organism fingerprinting. In SERS spectroscopy, it is of crucial importance to develop systems of interacting metal nanostructures capable of producing high field enhancement values with highly reproducible characteristics. Presently, the best approaches to generating efficient SERS sensors rely on random ‘roughening’ of metal surfaces by etching or by colloidal synthesis. Although this methodology recently enabled the demonstration of single-molecule SERS spectroscopy, it suffers from a lack of engineering design rules and deterministic optimization. Following the DANS approach, we have engineered plasmonic substrates for SERS biodetection and demonstrated ‘structural enhancement effects’ using photonic-plasmonic coupling over broad frequency spectra.

In particular, we showed that far-field diffraction in aperiodic arrays of metal nanoparticles plays an important role in
Figure 3. Top left: Pictures of experimental setup for dark-field colorimetric sensing with microfluidic-integrated deterministic aperiodic nanostructures (DANS) substrates, packaged microfluidic DANS sensor, and SEM picture showing a detail of a Rudin-Shapiro array of closely spaced (15 nm separation) Au nanodisks (30 nm height, 200 nm diameter). (a) Experimental surface-enhanced Raman scattering (SERS) spectra of p-mercaptoaniline (pMA, a surface probe molecule) on lithographically defined arrays of different separations. (b) Plasmon-enhanced linear scattering shift of microfluidic-integrated DANS substrates. (c) Variation of autocorrelation functions (ACF) of the scattered radiation from microfluidic-integrated DANS sensors immersed in a liquid with varying refractive index. L/L₀: Normalized sample length measured from the center of the array along its side. (d) Measured dependence of the autocorrelation functions of the scattered radiation in a microfluidic channel as a function of the liquid refractive index.

The formation of broadband and wide-angle photonic-plasmonic scattering resonances and that the interplay with near-field plasmonic interactions leads to efficient Raman sensing of molecular monolayers with high reproducibility and control of hot-spot locations. Moreover, we introduced a class of SERS substrates, called ‘aperiodic nano-galaxies,’ in which aperiodic metal nanoparticle arrays fabricated by EBL are coupled to smaller satellite nanoparticles by in situ chemical reduction. The resulting aperiodic structures feature multiple length scales and produce cascade enhancement (i.e., nanolensing) of SERS signals that significantly boosts sensitivity to almost single-molecule levels. The resulting aperiodic structures are composed of metallic nanoparticles of different separations and sizes (i.e., multiscale structures). When the larger particles are illuminated by an optical beam of the appropriate frequency, the incident electromagnetic field is enhanced by the resonant excitation of LSPs. Under this condition, the smaller particles interact with the already enhanced local fields created by the larger ones, giving rise to even larger values of enhancement factors in a cascade process that boosts the sensitivity of SERS detectors to almost single-molecule levels.

We believe that spatial (i.e., colorimetric) and frequency-based (i.e., elastic and Raman scattering) optical DANS sensors will be integrated on the same chip in the near future, creating multidimensional arrays of useful sensing information for a number of applications in biodetection, molecular biology, and biorecognition. Discrete components have recently been demonstrated: see Figure 3(a-d).

It is clear that the engineering of deterministic aperiodic structures in nanophotonics provides novel and exciting opportunities for optical physics and biosensing. As rapid progress continues in computational electromagnetics techniques, nanofabrication, and optical characterization, we envisage the optics of aperiodic media becoming essential for engineering more efficient devices to manipulate and enhance nanoscale light-matter interactions. We are currently working to integrate

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spatial-spectral sensors onto microfluidic platform technology to engineer rapid and reliable ‘optical responders’ to counter a broad range of diverse microbial, explosive, and chemical threats. By manipulating the responder’s surface we are targeting a specific set of analytes. Using lithographic and nanoimprinting fabrication techniques, we will integrate many colorimetric responders into a small area, enabling the sensor to monitor several different analytes in parallel. In addition, by engineering SERS substrates to control the location of sub-wavelength hot spots, we will optically extract spatially resolved chemical information on the composition of cell surfaces, which will enable us to monitor activities and interactions of research and health interest.

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References