3D Position Nanometrology of a Coronavirus-like Nanoparticle with Topologically Structured Light

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Abstract: Scattering of topologically structured light is highly sensitive to the position of a scattering object. We show that the position of a coronavirus-like 100 nm polystyrene sphere can be measured optically with deeply subwavelength accuracy.

Viruses are too small to be seen with a conventional optical microscope. They can be imaged with atomic force and cryo-electron microscopes, but AFM is slow and intrusive while cryo-EM is extremely expensive and only works with samples in matrices at low temperatures. No *in-vivo* imaging techniques are available to see viruses. To do so is crucial for disease control. How a virus settles and where it is located on different surfaces, from household cutlery to biofilms or membranes, is key information required for the development of disease control strategies and monitoring anti-microbial agents.

Topologically structured light fields can contain highly localized intensity hotspots, phase singularities, zones of energy backflow and high gradients of phase at dimensional scales orders of magnitude smaller than the wavelength of light. Here, we show that topological light fields – specifically 'super-oscillatory' fields, generated by precise interference of multiple waves diffracted on purposely designed intensity and phase masks – can be used to measure the position of a subwavelength dielectric nanoparticle in three dimensions via a deep learning-enabled analysis of the particle's scattering intensity patterns.

Our approach exploits changes in the scattering patterns that arise when the subwavelength object interacts with rapid spatial variations of the incident topological field. A deep learning process with a neural network trained on *a-priori* known positions of a nanoparticle is used to analyze scattering patterns for the determination of unknown particle positions.

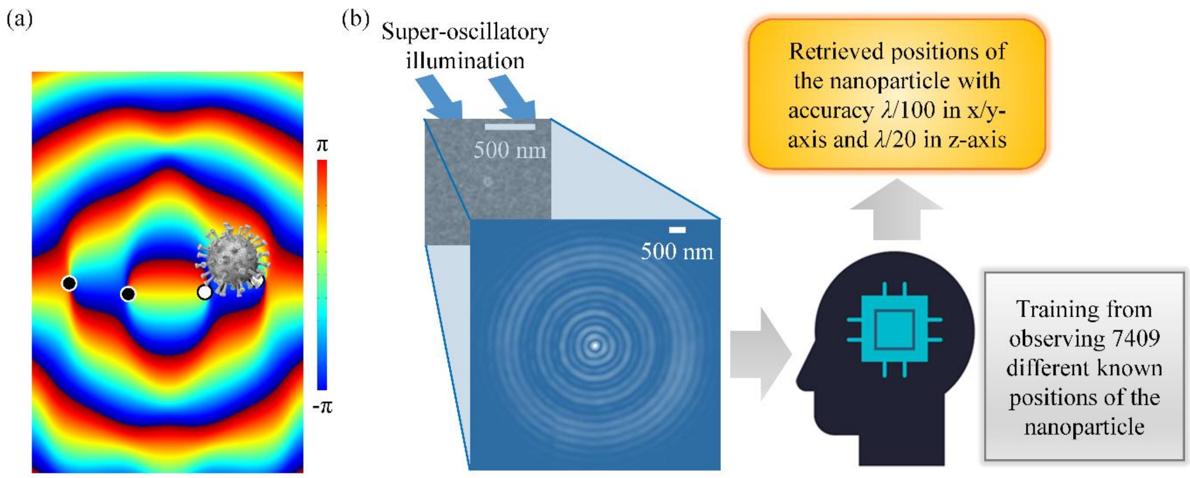

Fig. 1 (a) Cross-sectional phase profile of a super-oscillatory, topologically structured, coherent optical field. Singularities are indicated by circles (a black circle when the phase increases from -π to π by circling around the singularity clockwise; a white circle when it decreases). A coronavirus particle schematic, to scale, is overlaid. (b) Methodology for 3D positional nanometrology of a nanoparticle with topologically structured light. The particle is illuminated by super-oscillatory light and its diffraction pattern is recorded at a distance of a few wavelengths from the object. The diffraction intensity patterns are analyzed by a convolutional neural network. The trained network is able to determine particle positions with an in-plane accuracy of λ/100 and accuracy of λ/20 in the direction of light propagation.

We experimentally demonstrate 3D positional measurements for a 100 nm spherical polystyrene particle – representing, by size and organic polymer composition, a coronavirus particle. Our sample is prepared by drop-casting polystyrene particles with a diameter of 100 nm onto a glass substrate. Isolated particles are then located in scanning electron microscope images (Fig. 1b). The sample is illuminated, and scattered light is collected in transmission via pair of 100×, NA = 0.9 microscope objectives. The intensity and phase profile of the incident light field, at a wavelength λ = 488 nm is controlled by a pair of spatial light modulators. Scattered light is imaged in the far field using a 16-bit camera. Using a piezoelectric translation stage, the superosciallatory focal spot is scanned over a 400 (~0.82 λ) × 400 × 400 nm cubic volume with an interval of 20 nm, acquiring a scattering image at each point. From this library of 9261 images, 80% (selected at random) are used for training of a convolutional neural network, 10% as the validation dataset, and 10% for testing – i.e. retrieval of the particle position based on the image by the trained network.

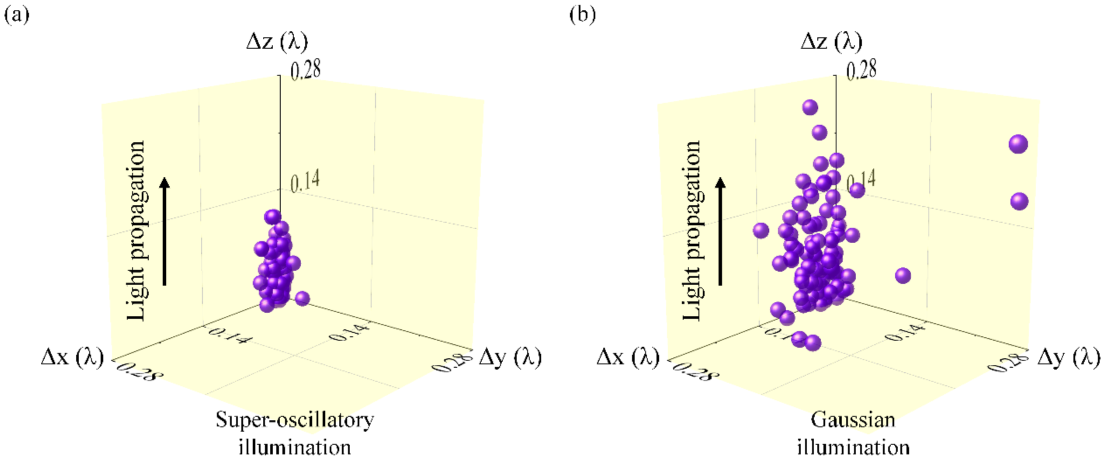

Fig. 2 Comparison of positional errors in optical measurements of the 3D coordinates of a coronavirus-like nanoparticle – a 100 nm polystyrene sphere between (a) super-oscillatory and (b) Gaussian illumination regimes. Each purple dot indicates the absolute value of the difference between the optically measured and ground truth positions of the nanoparticle. Incident light propagates along the *z*-axis.

Figure 2 shows the discrepancy between optically measured and ground truth positions of the nanoparticle, for both superoscillatory (Fig. 2a) and Gaussian focal spot (2b) illumination. Each purple dot indicates the absolute value of the 3D difference between measured and actual position for 93 randomly selected positions. We achieve measurement accuracies (standard deviations between measured and actual positions) of order 5 nm (λ/100) in the in-plane (x and y) directions, and 25 nm (λ/20) in the light propagation direction (z). In comparison, with simple Gaussian illumination, the accuracy is only 25 nm (λ/20) in the xy plane and 44 nm (λ/11) in the z-direction.