Drawing on the unique properties of entangled photons, quantum approaches can overcome the limitations of classical methods, enhancing spatial resolution, reducing stray light and suppressing shot noise.

The quantum imaging team at the Caltech Optical Imaging Laboratory. From left: Xin Tong, Zhe He, Lihong Wang and Yide Zhang.

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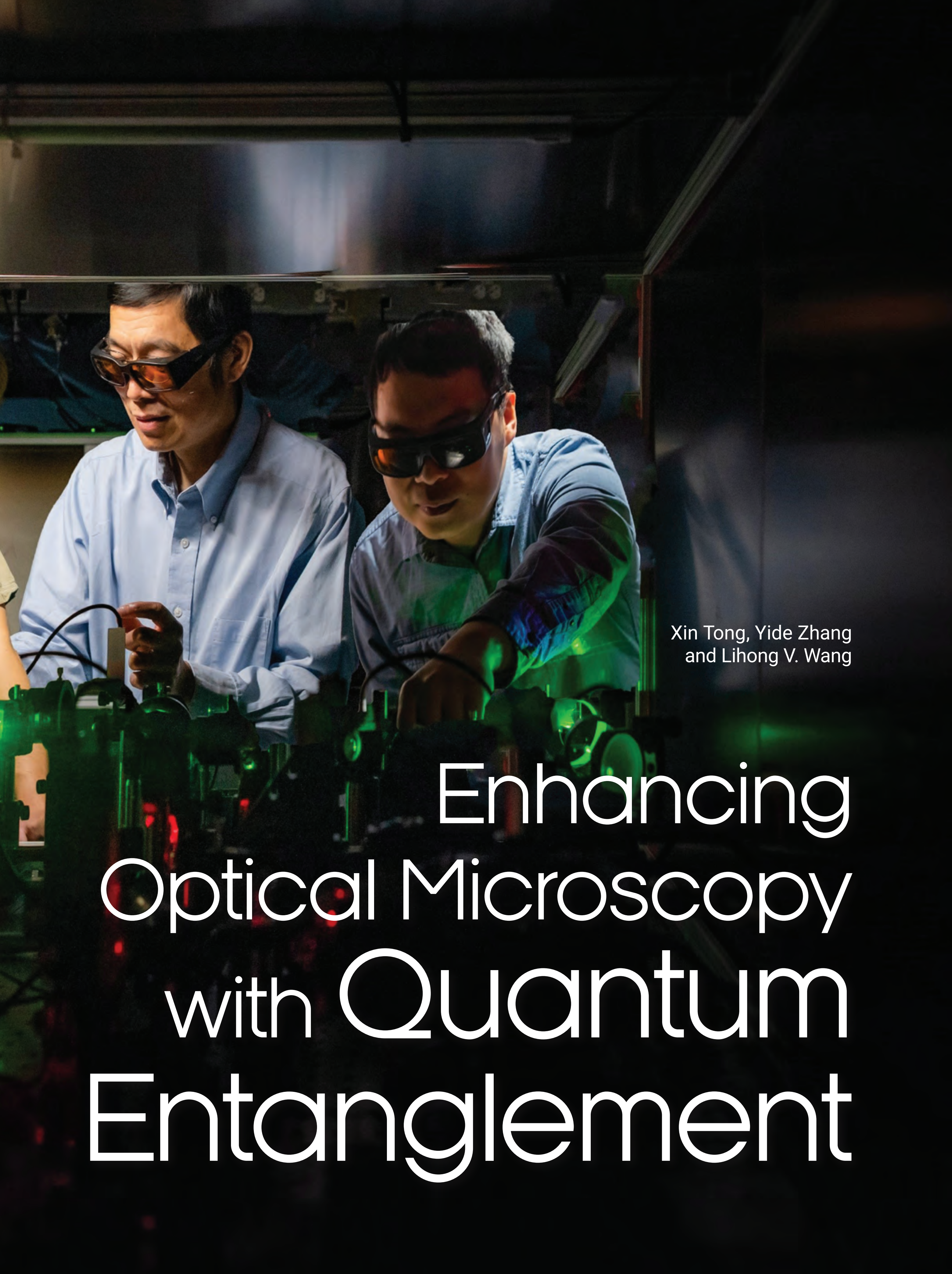

Xin Tong, Yide Zhang
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Enhancing Optical Microscopy with Quantum Entanglement

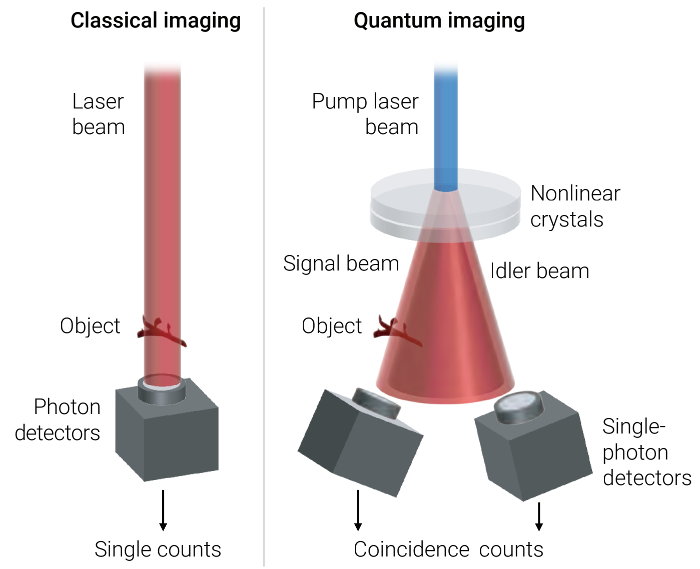
Ever since Antonie van Leeuwenhoek's first microscope in the 17th century, optical imaging has been widely used to noninvasively investigate the structures and dynamics of physical and biological systems. The interaction of nonionizing light with molecules provides rich molecular information about biological samples, aided by the convenience and compactness of optical systems. Optical imaging has thus served as the workhorse behind a wide variety of discoveries by biological researchers and medical practitioners.

An optical imaging system's performance is evaluated based on factors such as spatial resolution, contrast and noise. Spatial resolution, determined by the optical system's ability to distinguish between two closely spaced points, is fundamentally limited by the wavelength of the illumination photons and the numerical aperture of the imaging lens. Contrast—the difference in intensity between an object and its background—is essential for distinguishing features in the sample. The noise level of an image affects the microscope's sensitivity to detect weak signals and is determined by factors such as the sensor dark count and photon counts. The contrast-to-noise ratio (CNR) quantifies the ability to discern a target at the given spatial resolution.

To take these systems further, a new discipline has recently emerged—quantum imaging (QI). These imaging approaches take advantage of the properties of entangled or squeezed photons. A QI system typically involves an entangled-photon source, imaging optics and single-photon detectors, under experimental designs using paired photons to form microscopic images that exhibit advantages difficult or impossible to achieve via classical methods.

Ghost imaging and undetected-photon imaging, for example, provide spatial resolution using light that has not directly interacted with the object. Quantum holography achieves remote phase imaging with high spatial resolution and stray-light resistance. Super-resolution quantum microscopy, a recent development, allows detailed observation of cellular structures using low-intensity light. Coincidence detection of entangled photons can even potentially enable remote polarization measurement of an object light years away from the detectors.

As quantum sources, single-photon detection and reconstruction algorithms advance, we believe QI could have a huge impact on fields that rely on microscopic resolution or remote sensing. This article takes a look at QI's principles, techniques and applications—highlighting its transformative potential.



Typical classical imaging and quantum imaging compared.

Principles of quantum imaging

As the name implies, QI leverages quantum principles to enhance traditional imaging systems. At its core is the concept of quantum entanglement, in which two or more particles become linked such that measuring the quantum state of one particle directly affects the state of the other, regardless of the distance between them. This apparent "spooky action at a distance" (*spukhafte Fernwirkung*), in Einstein's words, cannot be explained by classical physics—but can still be harnessed to enhance imaging techniques.

In classical imaging (CI), photons are transmitted through the object to be imaged and reach a single detector. QI, in contrast, requires two detectors (or two regions on the same detector). Entangled photon pairs, generated through nonlinear crystals pumped by a laser beam, travel together, typically with some angular separation. One, the signal beam, passes through the object before hitting the detector; the other, the idler beam, is directly detected without interacting with the object. Rather than collecting single counts as in CI, QI requires time-resolved coincidence detection to distinguish truly entangled photon pairs from accidental counts. The images formed from coincidence counts (the QI images) are then compared with those formed only from single counts (the CI images).

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A quantum-imaging system uses paired photons to form microscopic images that exhibit advantages difficult or impossible to achieve via classical methods.

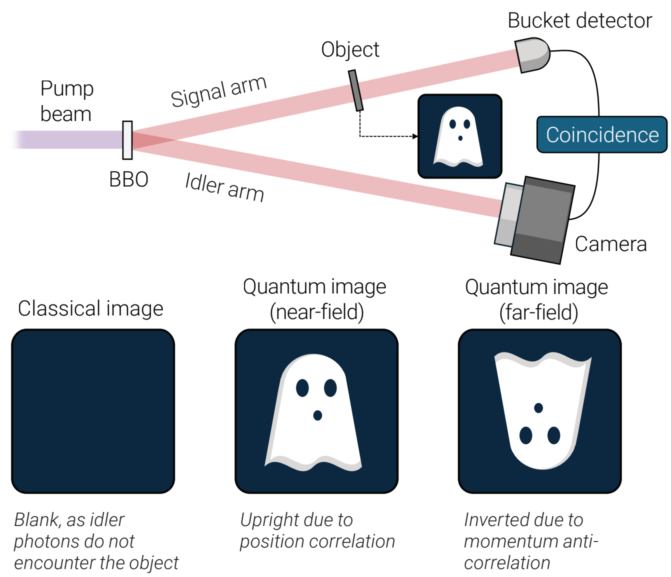
Quantum sources and detectors

In general, entangled photon pairs are generated through spontaneous parametric down-conversion (SPDC). In SPDC, a high-energy pump photon sent through a nonlinear optical crystal spontaneously splits into a pair of lower-energy entangled photons, based on energy and momentum conservation. The materials used for SPDC are non-centrosymmetric crystals like beta-barium borate (BBO), lithium niobate and potassium dihydrogen phosphate (KDP). These materials show strong χ^2 properties that facilitate efficient down-conversion of the pump photons. The choice of crystal and its configuration (for example, periodically poled) determines the SPDC efficiency and wavelength range.

Based on the polarization of the emitted photons, SPDC sources can be categorized as follows: Type 0, in which the signal and idler photons have polarizations parallel to the pump photon; Type I, in which the signal and idler photons have polarizations perpendicular to the pump photon; and Type II, in which the signal and idler photons have orthogonal polarizations. Polarization entanglement can be achieved by stacking two Type 0 (or Type I) crystals with orthogonal optical axes or using the intersections of Type-II SPDC outputs.

Furthermore, SPDC sources can be configured in collinear or noncollinear setups, depending on the relative directions of the emitted photons. SPDC sources also can be degenerate (producing photon pairs with identical wavelengths) or nondegenerate (producing photon pairs with different wavelengths). Nondegenerate sources are useful for applications requiring different wavelengths for different parts of the experiment, such as in quantum spectroscopy or imaging with undetected photons.

Characterizing entangled-photon sources involves measuring the degree of entanglement in terms of spatial (position–momentum), energy–time and polarization correlations. These characterizations are crucial for optimizing the performance of QI systems. Spatial entanglement, for instance, is evaluated by measuring the correlations in the positions and momenta of the photon pairs—essential for applications like super-resolution imaging and quantum lithography.



Ghost imaging

In ghost imaging, photons in the signal arm pass through the object being imaged, while corresponding entangled photons in the idler arm pass directly to the detector.

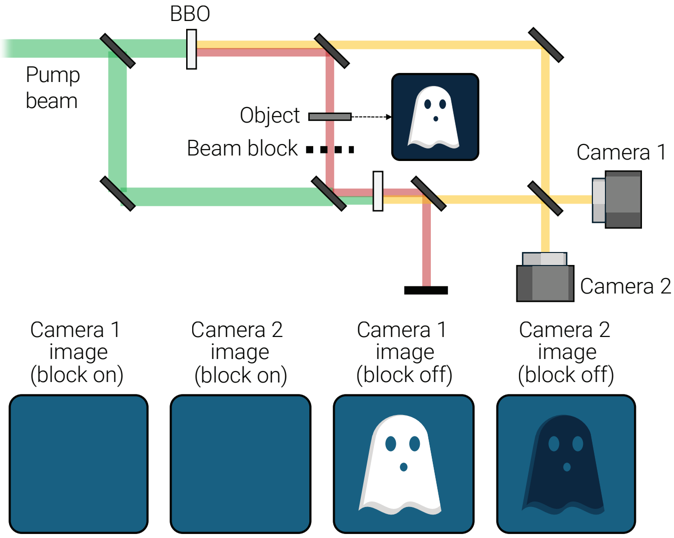
Detection of entangled photons involves single-photon detectors and coincidence detection. For photon detection, single-photon avalanche photodiodes (SPADs) and superconducting nanowire single-photon detectors (SNSPDs) are commonly used as bucket detectors, while SPAD arrays, electron-multiplying CCDs (EMCCDs) and scientific CMOS (sCMOS) detectors can be used as spatially resolved single-photon cameras. The detector outputs are converted to coincidence counts via hardware (such as time-resolved coincidence counting systems) or software (such as statistical reconstruction algorithms).

Quantum-imaging techniques

QI utilizes a variety of techniques to push imaging capabilities beyond classical limits—each offering specific advantages in spatial resolution, stray-light resistance or shot-noise suppression.

Ghost imaging

In ghost imaging, spatial resolution is provided using light that has never directly interacted with the object. Signal photons are detected by a bucket detector, which



Undetected-photon imaging

Schematic of the undetected-photon imaging setup, with images acquired by the two cameras when the beam block is on or off. The last two images are complementary in intensity due to conservation of energy between the two cameras.

does not provide spatial resolution, while the idler beam is captured by a spatially resolved camera. By measuring the correlations between the two beams, an image of the object can be reconstructed.

Ghost imaging can be configured using position (near-field) or momentum (far-field) correlations, and can be performed using both quantum entangled photons and classical thermal light. This technique is particularly useful in situations where direct imaging is challenging or impossible.

Undetected-photon imaging

Undetected-photon imaging takes advantage of quantum interference to form an image without detecting the photons that have interacted with the object. In this method, a pair of entangled photons is generated, with one photon interacting with the object and the other serving as a reference. The image is formed by measuring the interference pattern of the reference photons, which indirectly contains information about the object. This approach can help when imaging at wavelengths for which detectors are inefficient or unavailable, as it allows the use of different wavelengths for illumination and detection.

Imaging through noise

Another technique using correlations between SPDC photon pairs—in this case to reject stray light—is imaging through noise. The correlations allow QI protocols to select correlated photon events while rejecting uncorrelated background fluctuations and sensor noise events. By performing coincidence detection of photon pairs using either time gating or pixel-wise correlation-based reconstruction, QI can substantially suppress stray light and sensor noise.

Sub-shot-noise imaging

As its name suggests, sub-shot-noise imaging aims to surpass the shot-noise limit—a fundamental limit in classical imaging that arises from the discrete nature of photons. Using entangled light, detectors arrayed in a two-arm configuration can exploit correlation and cancel the random fluctuation in two arms.

Similarly, using so-called squeezed light states, it is possible to reduce the noise in one quadrature (e.g., position or momentum; amplitude or phase) at the expense of increasing it in the orthogonal quadrature, thereby improving the signal-to-noise ratio in the quadrature of interest. This technique, used in LIGO detection of gravitational waves, is also useful for biological imaging under the low light doses needed to avoid phototoxicity or effects on the biological processes being observed.

Super-resolution quantum microscopy

In biological microscopy, QI techniques enhance resolution and sensitivity (that is, suppress noise), allowing researchers to observe cellular and molecular structures with more detail than via classical counterparts using the same optics. Super-resolution quantum microscopy uses entangled photons to achieve resolution beyond the diffraction limit of classical optics, a crucial capability for studying biological processes at the nanoscale, where traditional microscopy can fall short. Further, QI reduces potential photodamage to biological samples, as it can achieve high resolution using lower light intensities.

One form of super-resolution quantum microscopy is imaging by coincidence from entanglement (ICE), which uses spatial entanglement to enhance classical resolution by around 40%. The basic ICE experimental setup includes two SPADs and a pair of objective lenses for microscopic resolution. Here, spatial entanglement enables the idler arm to function as a "virtual pinhole" in the signal arm, forming virtual confocal microscopy that narrows the point-spread function (PSF).

In addition to resolution enhancement, ICE achieves 25 times greater suppression of stray light than classical imaging, making it highly effective for biological studies under low-intensity illumination and ambient lighting. The enhanced resolution and CNRs enable detailed

Super-resolution quantum microscopy uses entangled photons to achieve resolution beyond the classical diffraction limit, a crucial capability for studying biological processes at the nanoscale.

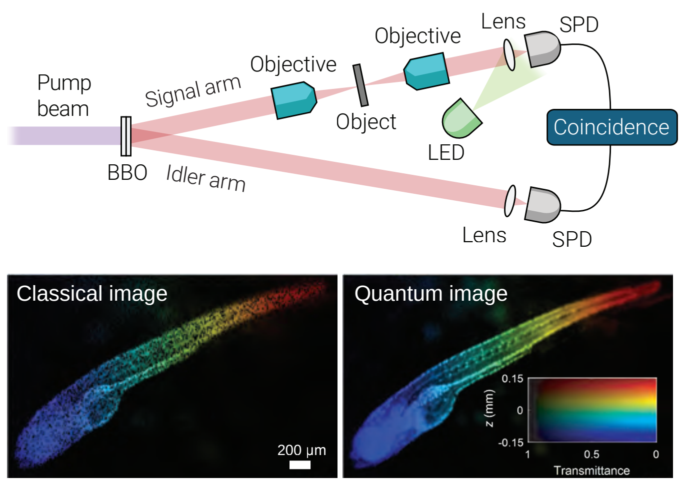
imaging of biological organisms. Additionally, ICE utilizes polarization entanglement to quantify full birefringence properties (such as phase retardation and refractive-index axis angles) of a biological sample without directly changing the incident beam's polarization state. This technique could even empower future applications in remote sensing, as measuring idler photons' polarization state equivalently varies the polarization state of the photon incident on the object, no matter how far the object is from the detectors.

ICE enhances the resolution by around 40%, or approximately $2^{1/2}$ (the standard quantum scaling with the square root of the number of quanta). However, given Heisenberg scaling (linearly with the number of quanta), near-100% resolution enhancement is possible using entangled biphotons. A technique demonstrated by our team in 2023, quantum microscopy by coincidence (QMC), achieves the Heisenberg scaling at microscopic resolution (see figure, p. 39). QMC involves wide-field illumination and a spatially resolved EMCCD camera. By balancing the optical path lengths of entangled photons, QMC effectively doubles the classical resolution for more detailed cellular imaging. QMC also increases imaging speed by five times and provides ten times greater resistance to stray light compared with existing QI techniques.

QMC's low-intensity, nondestructive illumination makes it ideal for bioimaging, as it can reveal cellular structures with unprecedented clarity. We believe QMC marks a major step forward in quantum-enhanced microscopy, pushing the boundaries of classical imaging.

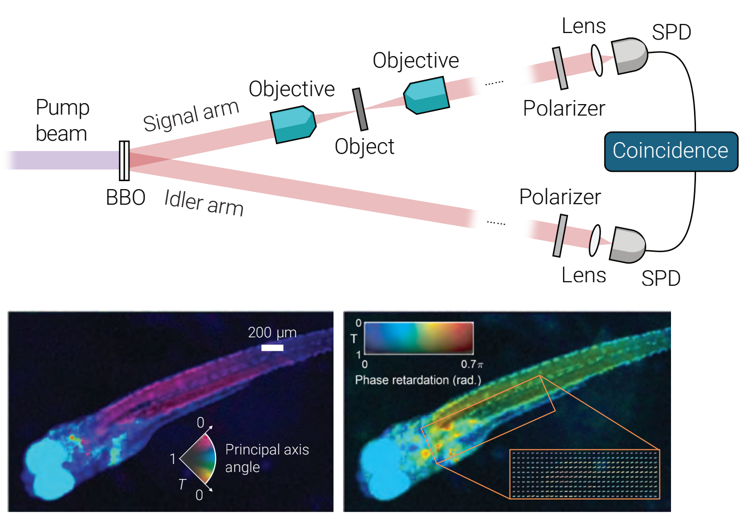
Quantum holography

Another QI technique that uses polarization entanglement to enable remote phase imaging, enhance imaging resolution and reduce noise is quantum holography. This method leverages spatially and polarization-entangled photon pairs to encode phase information, which is then retrieved through spatial intensity correlation measurements. Unlike classical holography,



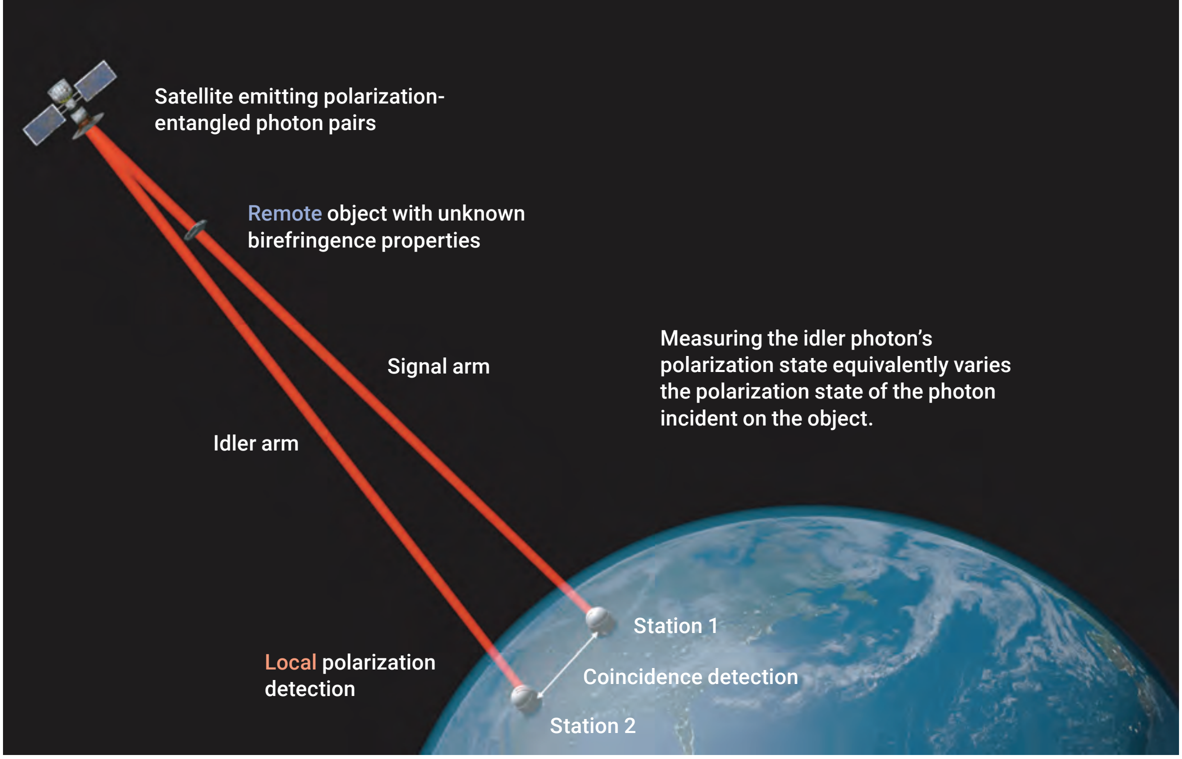
ICE: Quantum imaging through stray light

Top: Schematic of a quantum-imaging setup with stray-light (LED) contamination (SPD: single-photon detector). Bottom: While the classical image (left) is disrupted by the stray light, the quantum image (right) remains resistant to it, enabling more detail to be rendered.



ICE: Imaging birefringence via polarization entanglement

Top: A schematic of a typical ICE setup for polarization entanglement (SPD: single-photon detector). Bottom: Remote measurement of birefringence properties of a zebrafish, enabled by ICE.



ICE could enable polarization detection at long remote-sensing distances, through entanglement of signal and idler photons. .
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this approach does not require path overlap between reference and illumination beams and is resilient to dynamic phase disorders and stray light. In 2021, a research team from the University of Glasgow, UK, demonstrated a 1.84-fold resolution enhancement for quantum holography compared with classical holography.

Quantum holography enables high-resolution imaging of complex objects, including biological samples, and offers great potential for applications in quantum state characterization, such as measuring the Clauser–Horne–Shimony–Holt inequality to quantify hyper-entanglement. The approach's robustness and resolution benefits make it valuable for imaging in noisy environments and studying fine details in biological objects.

Quantum imaging's advantages and limitations

QI offers a compelling list of advantages:

Enhanced resolution. Spatial entanglement allows for super-resolution imaging, surpassing the classical diffraction limit—an essential advantage for applications requiring detailed imaging at microscopic or nanoscopic scales, such as fine details in biological objects.

Stray-light resistance. By rejecting stray light under low light doses (in setups like imaging through noise), quantum correlations enable the imaging of low-contrast objects that are difficult to capture with classical methods—a particular benefit for biological imaging, where detecting subtle differences without affecting the biological process is crucial.

Sub-shot-noise. Quantum techniques such as time-gated coincidence detection or squeezing can reduce shot noise to improve the image quality, lessening or removing a major limiting factor for classical imaging, especially when dealing with low-light conditions.

Wavelength conversion. Some biological objects are vulnerable under light of certain wavelengths (such as UV), and some detectors have higher sensitivity and lower cost at certain wavelengths. Degenerate SPDC allows for acquiring images with photons of doubled the harmful wavelength while maintaining the original resolution. Nondegenerate SPDC, via setups such as undetected-photon imaging, allows for imaging at wavelengths that are difficult to detect directly.

Remote-sensing possibilities. QI, including techniques such as quantum holography, could enjoy advantages for remote sensing, overcoming challenges such as the long separation of detectors from object and the difficulty in directly altering the incident beam properties in the signal arm.

While some advantages of QI over classical imaging can be emulated classically, others are uniquely quantum. For example, ghost imaging above sub-shot-noise, resistance to stray light and super-resolution at the standard quantum scaling (with the square root of the number of quanta) have been demonstrated using classical light sources. But QI breaks the classical limits

Quantum imaging breaks the classical limits by reaching the Heisenberg scaling and reducing shot noise, as well as remote manipulation of polarization.

by reaching the Heisenberg scaling (linearly with the number of quanta) and reducing shot noise, as well as remote manipulation of polarization. These capabilities make QI a potentially powerful tool for enhancing imaging performance in ways that classical techniques cannot match.

Notwithstanding these advantages, QI does still face several practical limitations. A significant one is the complexity and sensitivity of generating and maintaining quantum states such as entangled photons, which require precise experimental conditions and equipment. The need for advanced single-photon detectors and cameras adds to the cost and complexity of QI setups—as does the integration of QI into existing imaging systems, which often entails considerable modification and specialized components.

The low photon flux associated with limited SPDC efficiency (typically around 10^{-6}) and the requirement for minimizing double photon counts can lead to longer acquisition times for QI than for CI, making real-time imaging challenging. Another limitation is the scalability of QI techniques for larger or more complex objects, which requires massively parallel bright entangled-photon generation and efficient detection methods.

Addressing these limitations will be crucial for the broader adoption of QI in scientific and industrial applications. But when that broader adoption comes, we believe, the remarkable power of QI could well spur new scientific breakthroughs. OPN

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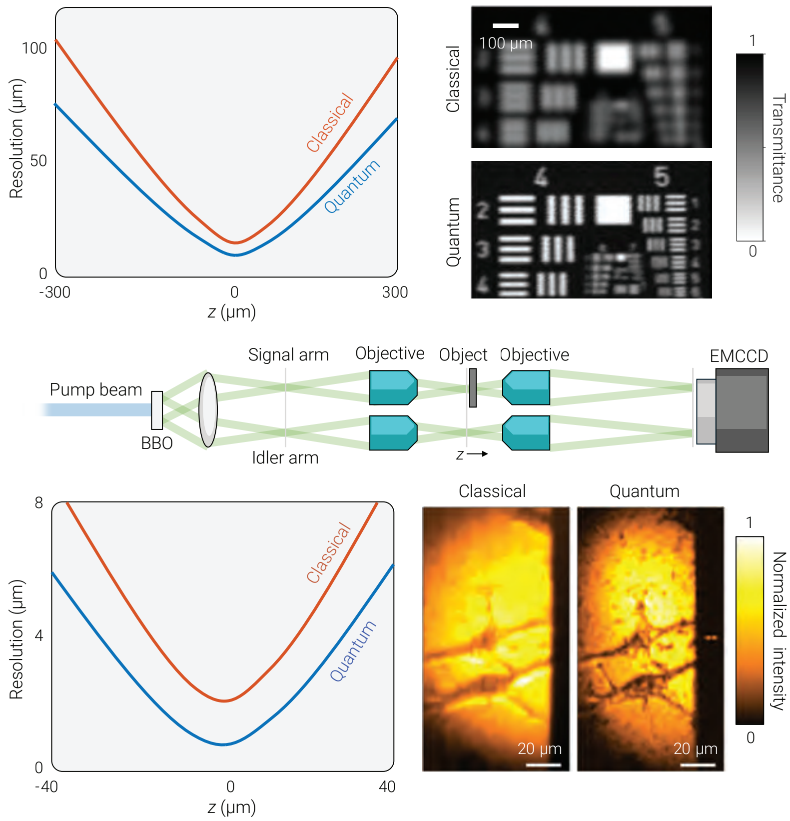

Super-resolution: ICE and QMC

Top: In super-resolution imaging, ICE can enable a roughly 40% resolution enhancement relative to classical imaging (left), as depicted in experiments with standard USAF resolution targets (right). Center: Schematic of the QMC setup. Bottom: QMC can enable 100% spatial-resolution enhancement (left) relative to classical imaging, enabling the detailing of delicate structures in cellular images (right).

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