Quantum Microscopy for Biomedicine
A real-world application of quantum imaging

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The visuals of this talk will be posted at boydnlo.ca/presentations

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Quantum Imaging

- The goal of quantum imaging is to produce “better” images using quantum methods
  - image with a smaller number of photons
  - achieve better spatial resolution
  - achieve better signal-to-noise ratio
- Alternatively, quantum imaging is research that seeks to exploit the quantum properties of the transverse structure of light fields

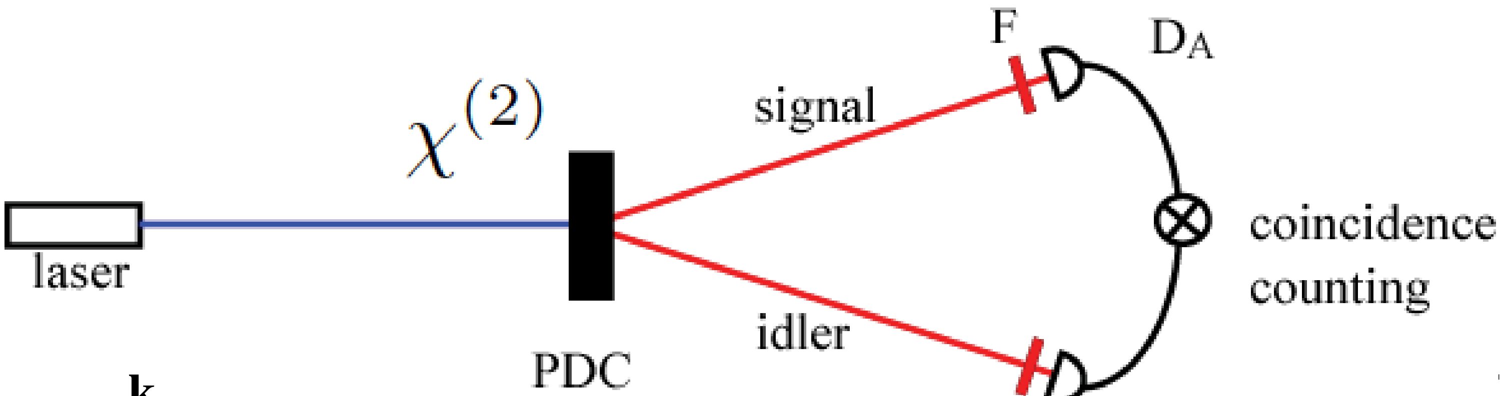
Quantum Imaging Outline

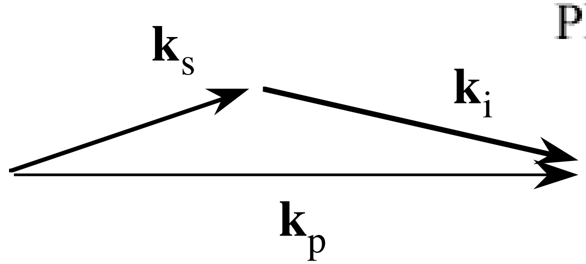
1. Introduction to Quantum Imaging
2. Quantum Microscopy for Biomedicine
3. Imaging through Strongly Scattering Media
4. Interaction-Free Ghost Imaging

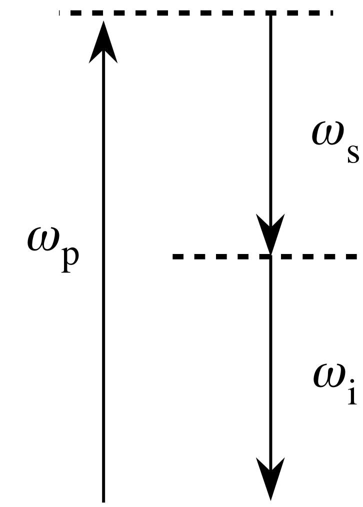
Why do we need quantum? (think of STED, etc.)

And what is "quantum"?

Parametric Downconversion: A Source of Entangled Photons







The signal and idler photons are entangled in:

(a) polarization

(b) time and energy (note different format of name)

(c) position and transverse momentum

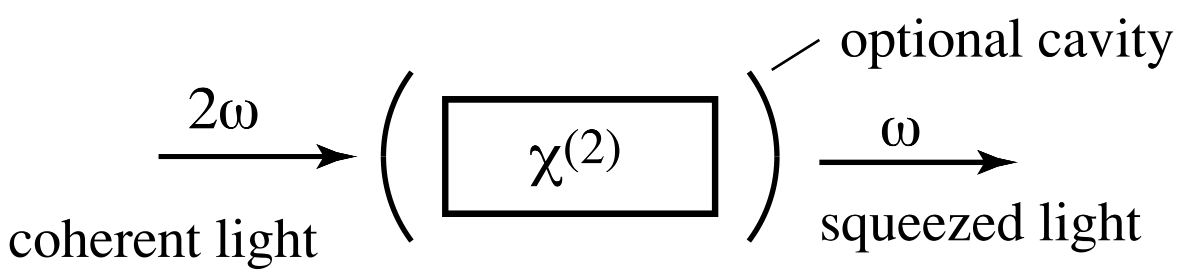
(d) angular position and orbital angular momentum

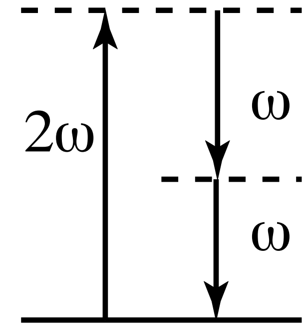
Entanglement is important for:

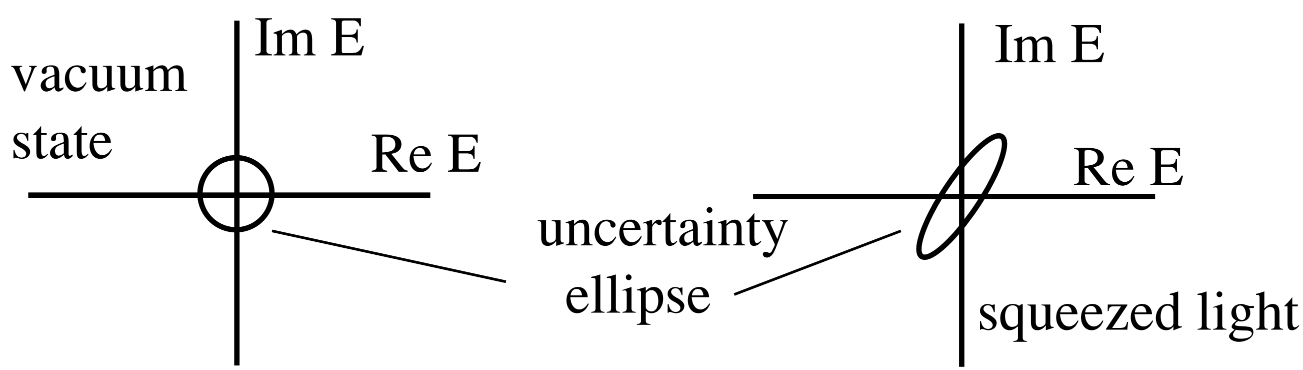
(a) Fundamental tests of QM (e.g., nonlocality)

(b) Quantum technologies (e.g., secure communications)

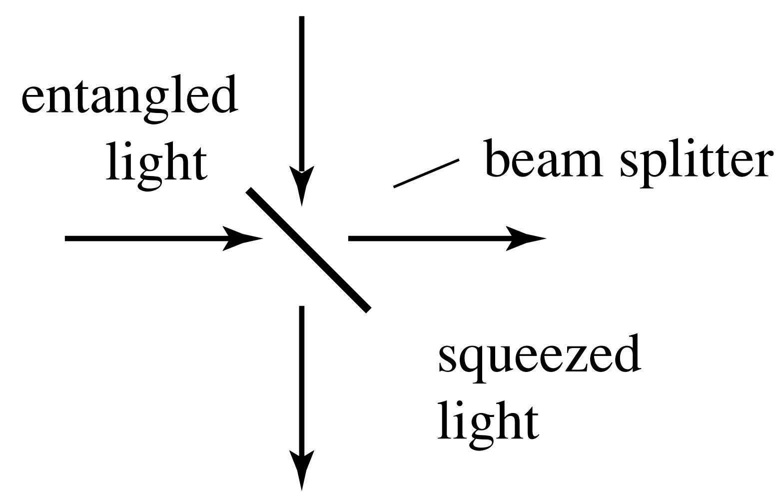
Squeezed Light Generation





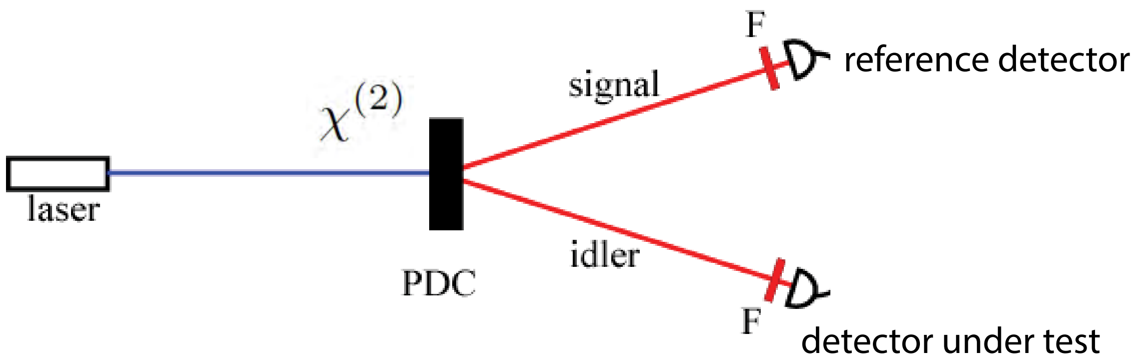


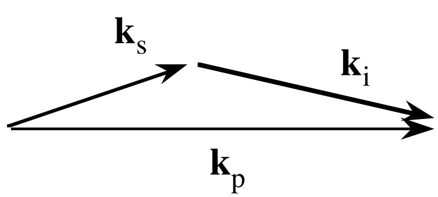
Entanglement and squeezing share a common origin. In fact:

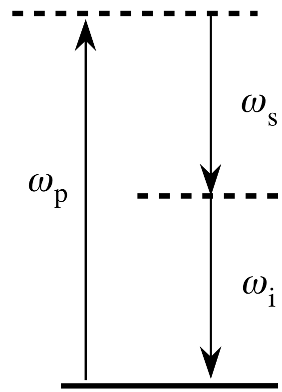


Klyshko's Method for Absolute Calibration of a Photodetector

- Absolute measurement of detector quantum efficiency (Klyshko, Sergienko, Migdall, Polyakov, etc.)





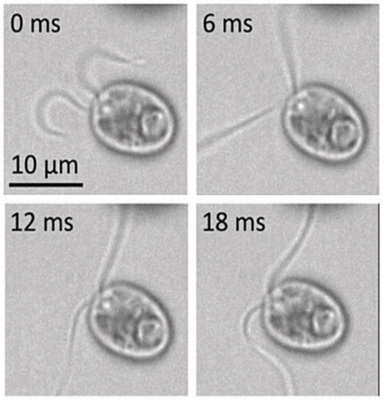


- Earlier work (Klyshko) established that the light produced by spontaneous parametric downconversion (SPDC) can be characterized in terms of the radiometric property known as brightness (or radiance).

Quantum Microscopy for Biomedicine

Many biological samples require low illumination intensities and long wavelengths

- Many biological materials suffer structural damage when exposed to strong laser light, especially at short wavelengths.
- Problem: Low-intensity imaging typically leads to a low SNR.
- Problem: Imaging with long wavelengths results in lower spatial resolution.
- Many biological materials display very low intensity contrast. Need to perform phase-sensitive imaging.

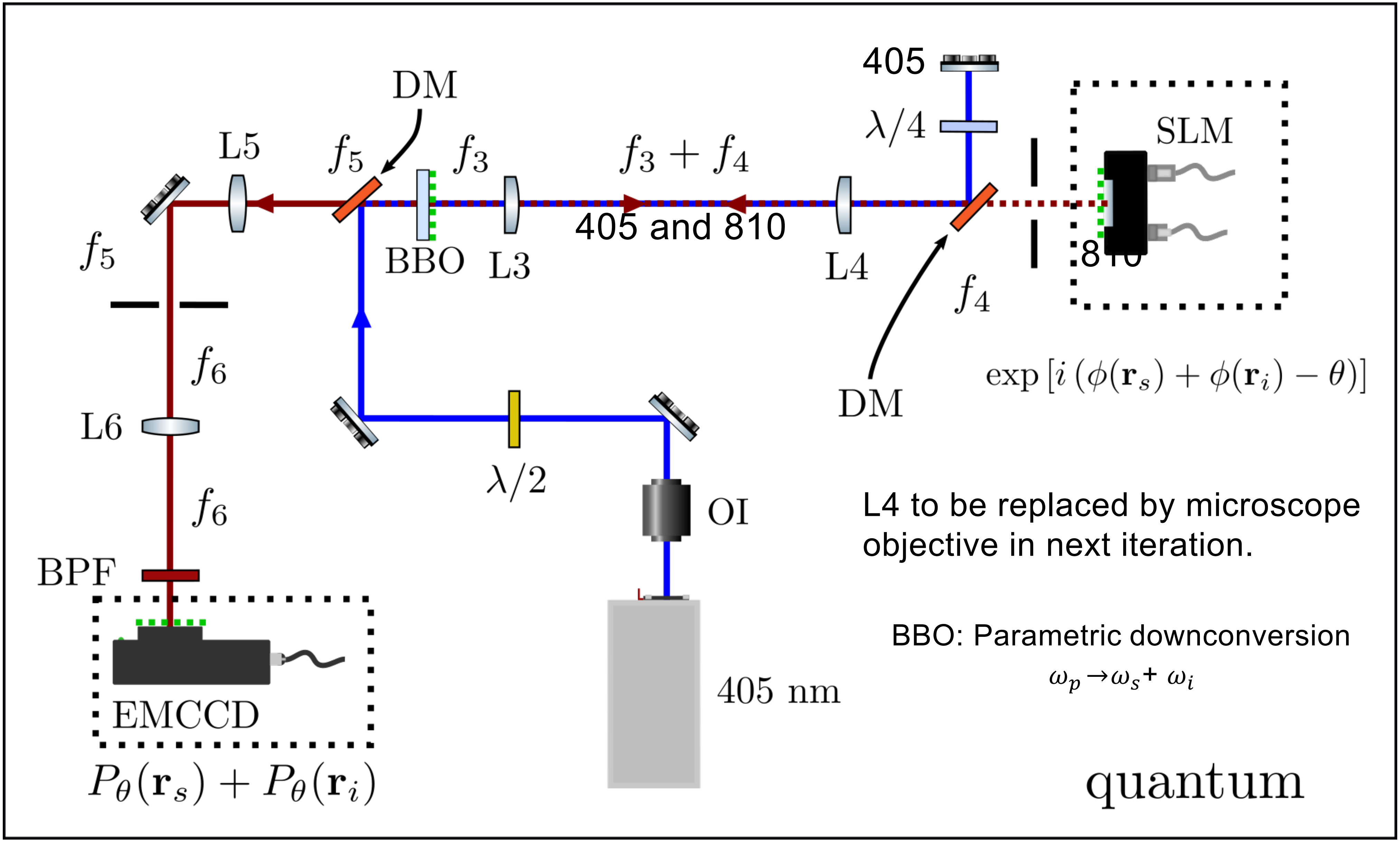


O. Taino et al., Soft Matter **17**, 145-152 (2021).

Solution:
Use quantum imaging.

[1] Y. Niwa et al., Proc. National Acad. Sci. **110**, 13666–13671 (2013).
[2] Q. Thommen et al., Front. Genet. **6**, 65 (2015).

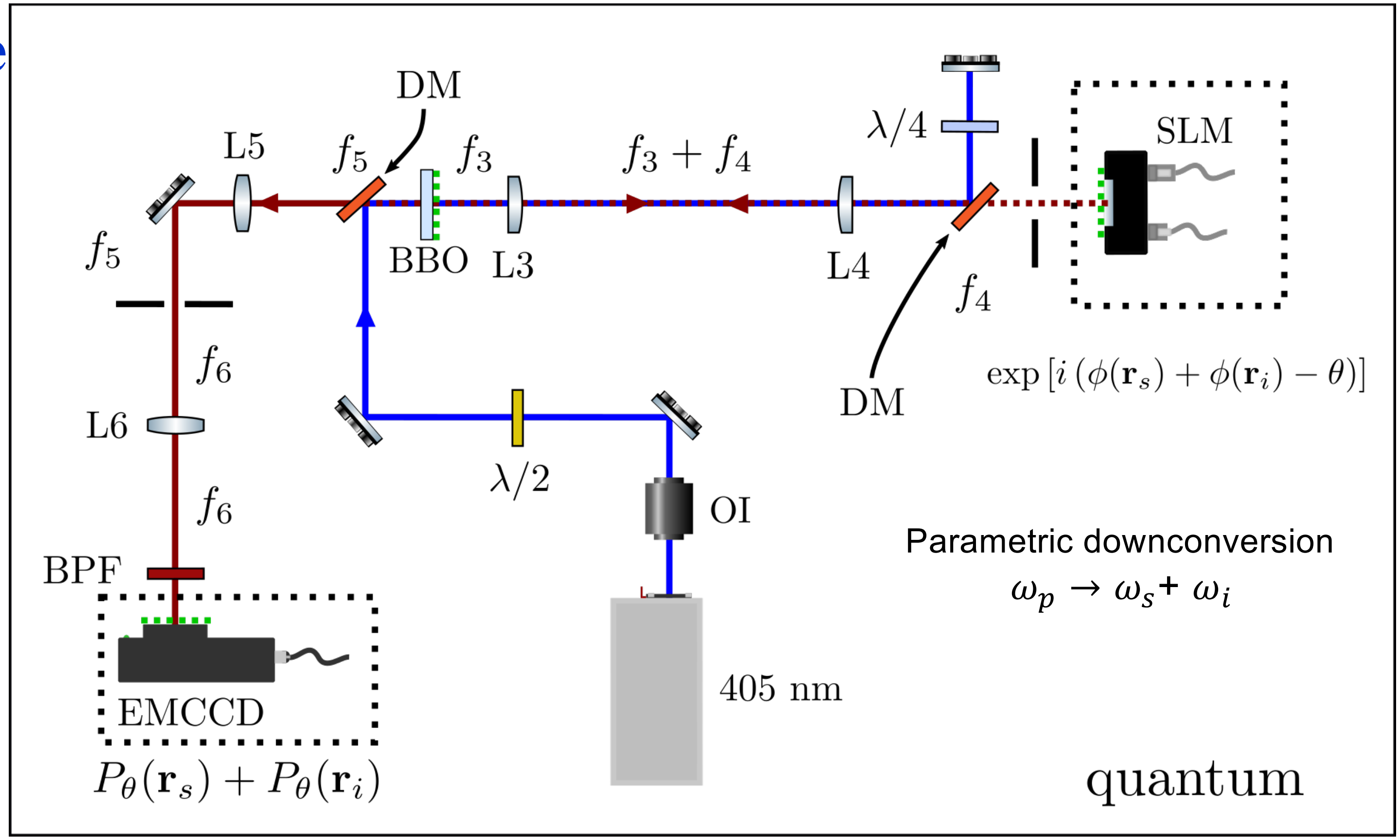
Phase-Sensitive Quantum Imaging Setup:



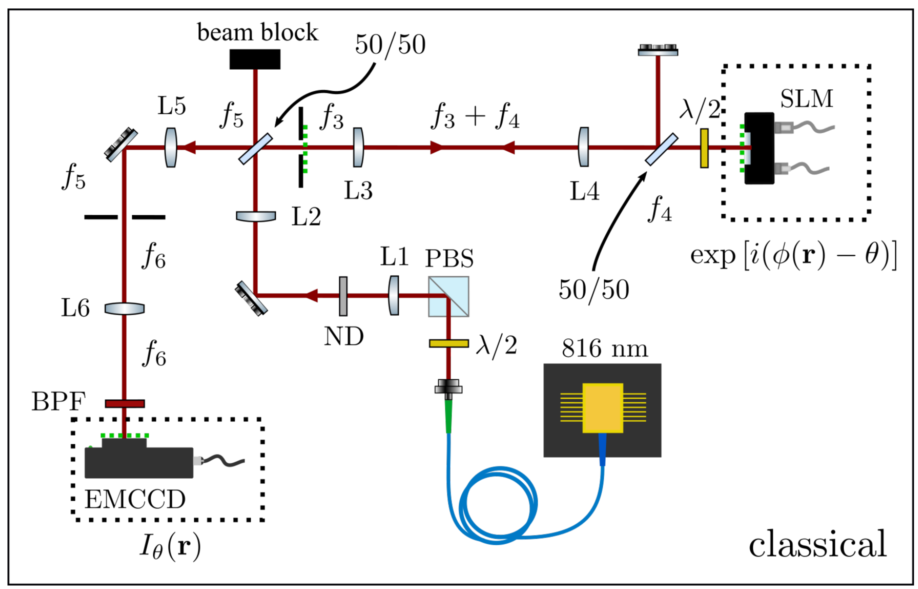
A. Nicholas Black, Long D. Nguyen, Boris Braverman, Kevin T. Crampton, James E. Evans, and Robert W. Boyd, "Quantum-enhanced phase imaging without coincidence counting," Optica 10, 952-958 (2023).

Our phase-sensitive imaging setups:

Quantum

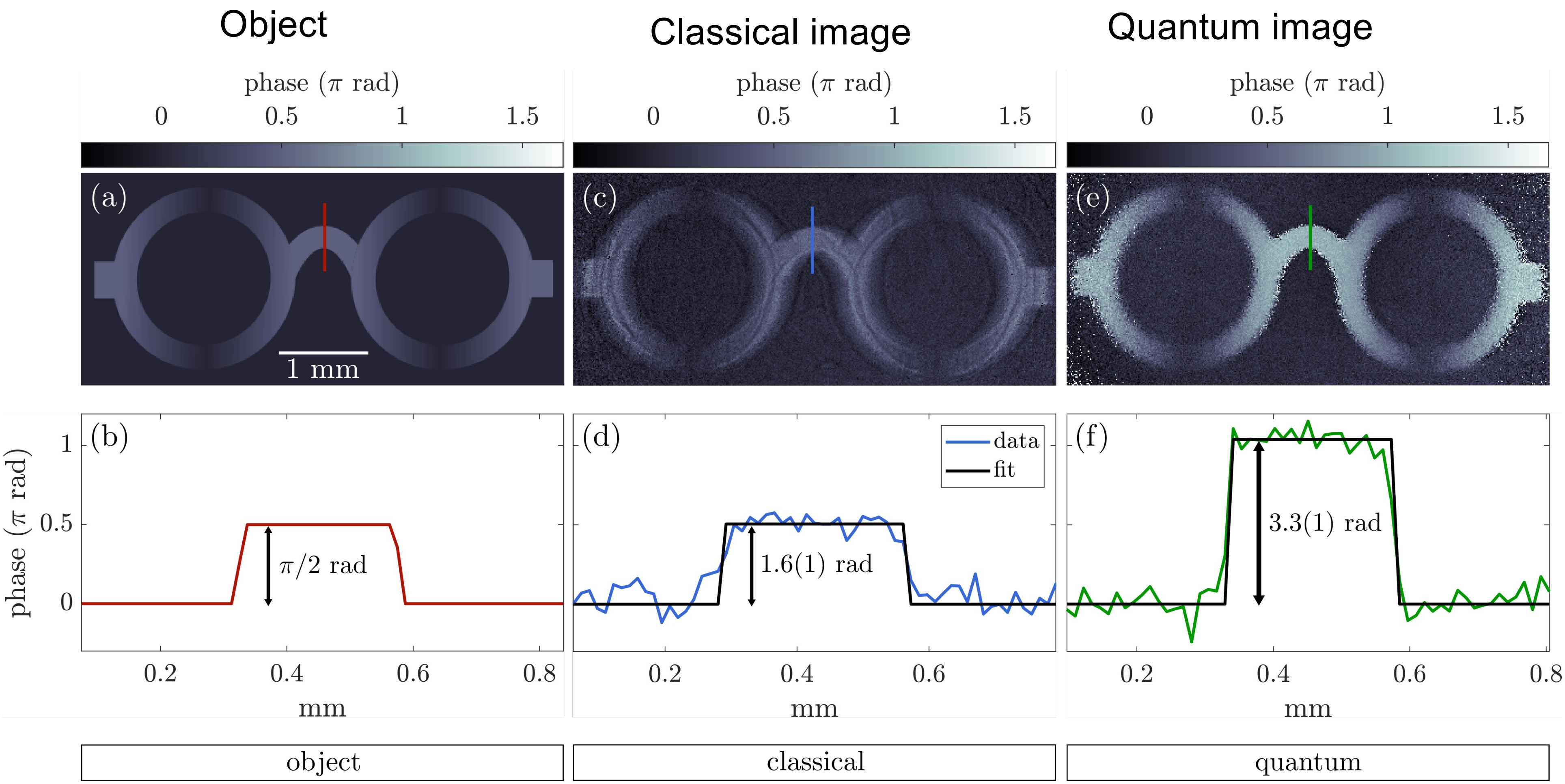


Classical
(with same numerical aperture)



A. Nicholas Black, Long D. Nguyen, Boris Braverman, Kevin T. Crampton, James E. Evans, and Robert W. Boyd, "Quantum-enhanced phase imaging without coincidence counting," Optica 10, 952-958 (2023).

Comparison of classical and quantum phase imaging



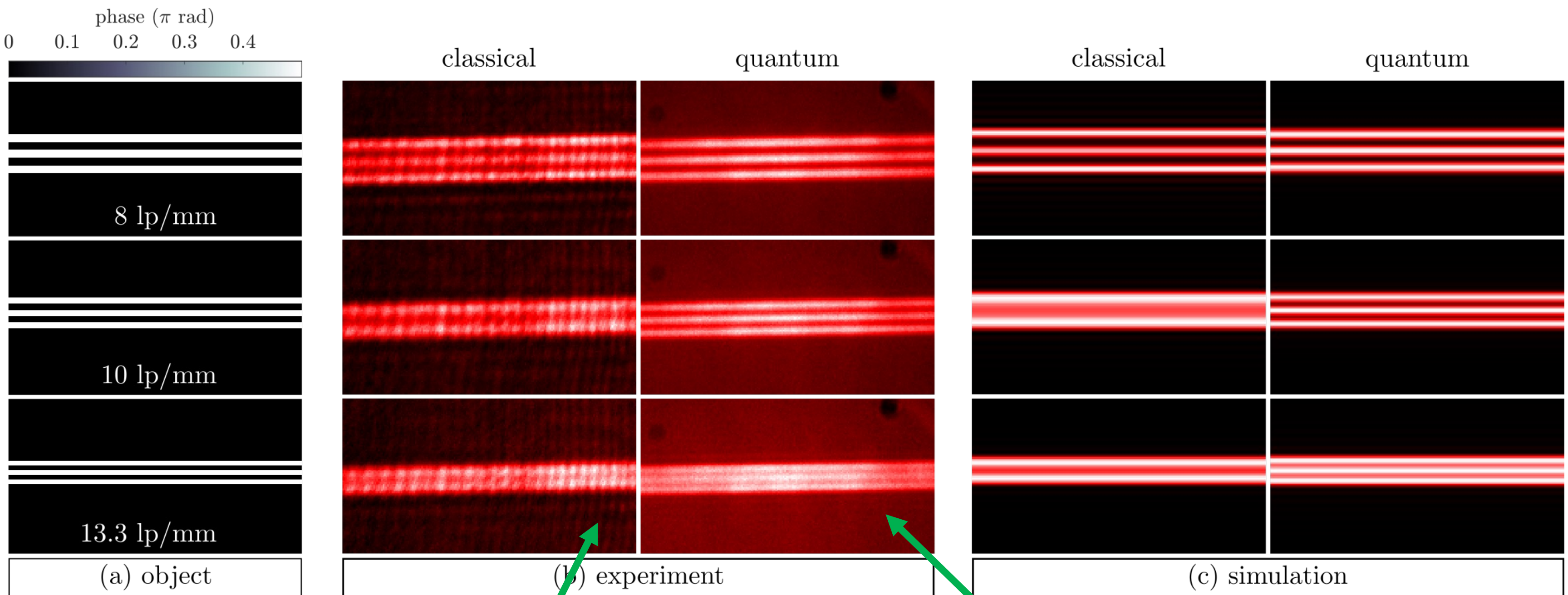
The “object” is a phase object written onto an SLM.
Photon flux: ~40 photons/s μm^2

Signal twice as large in quantum setup
Image is 1.7-times sharper in quantum setup

A. Nicholas Black, Long D. Nguyen, Boris Braverman, Kevin T. Crampton, James E. Evans, and Robert W. Boyd, "Quantum-enhanced phase imaging without coincidence counting," Optica 10, 952-958 (2023).

Monument In Tokyo, Japan

Comparison of quantum to classical spatial resolution



Vertical fringing is from back reflections.

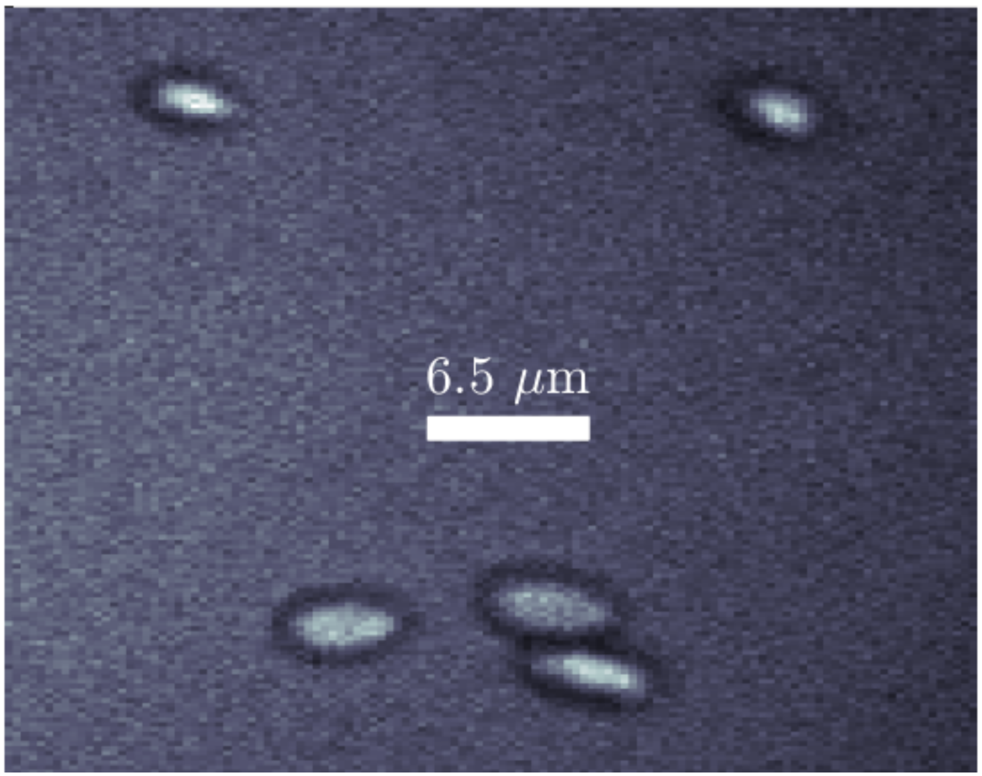
Fringing from back reflections not present in quantum experiment because back reflections are not mode matched.

The quantum experiment achieves ~1.7 times better spatial resolution.

A. Nicholas Black, Long D. Nguyen, Boris Braverman, Kevin T. Crampton, James E. Evans, and Robert W. Boyd, "Quantum-enhanced phase imaging without coincidence counting," Optica 10, 952-958 (2023).

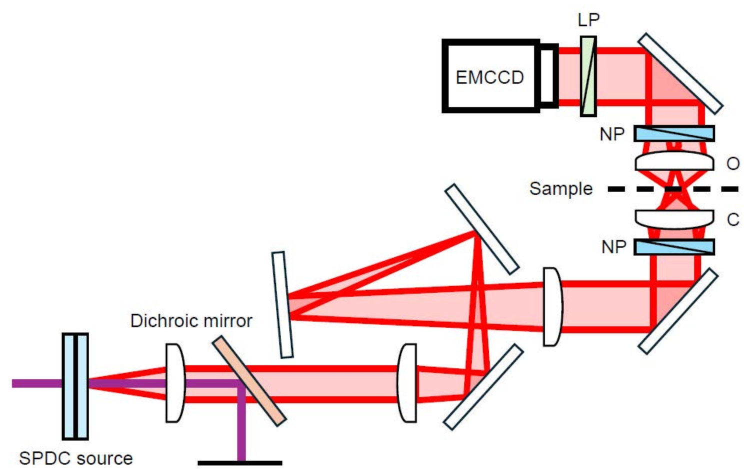
Latest Lab Result: Quantum Phase Microscopy

- Living yeast cells imaged by entangled photons at 710 nm.
- Image is near the Abbe limit of resolution



Objective: 40x magnification, NA = 0.75

Quantum Nomarsky microscope

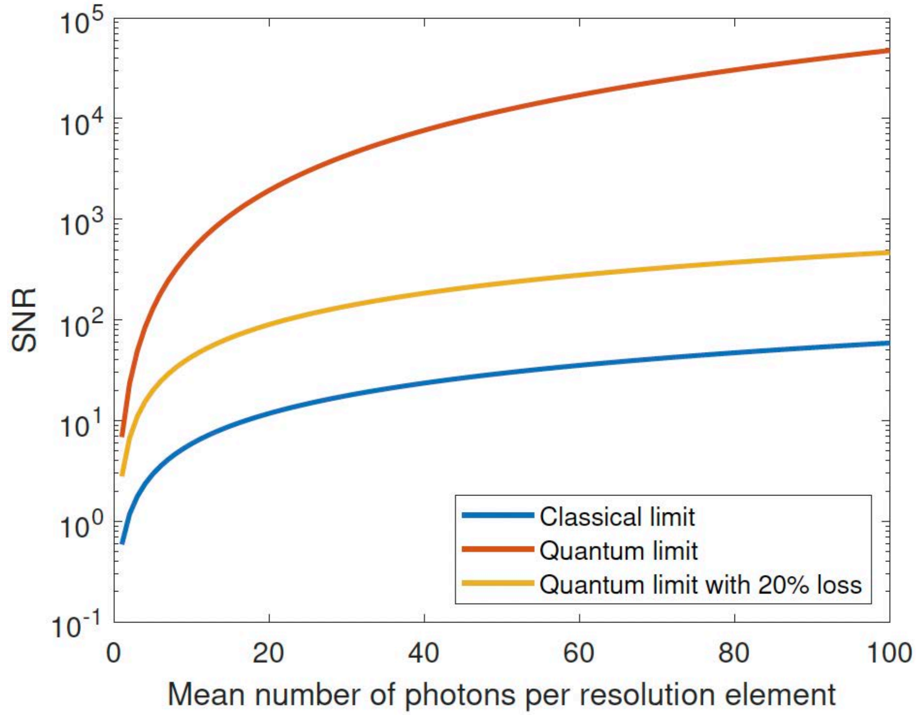


Progress is financially-limited.

Collaboration with US DOE Pacific Northwest National Laboratory

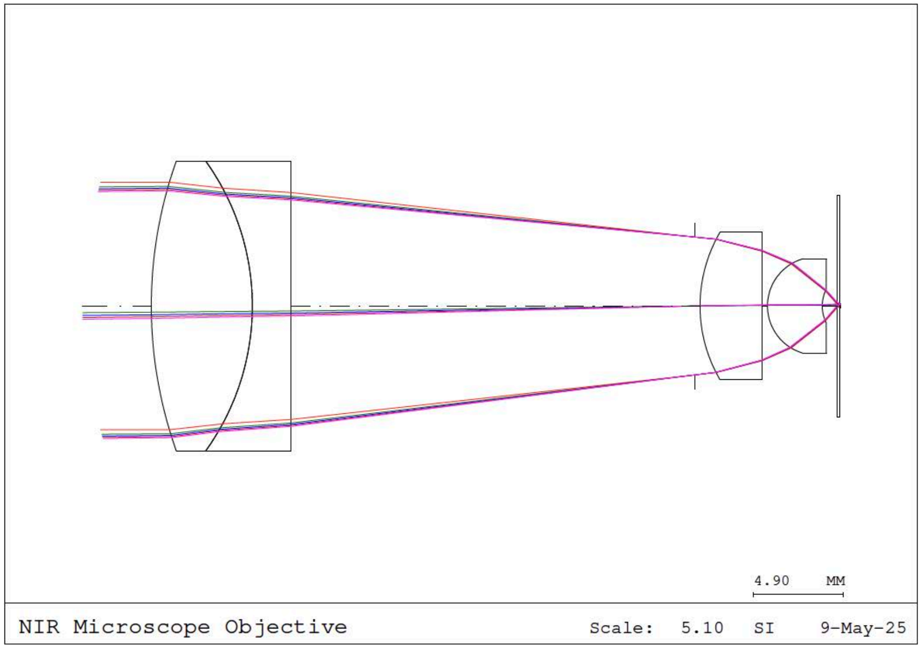
Next Step: Design and Acquire Custom Microscope Objective

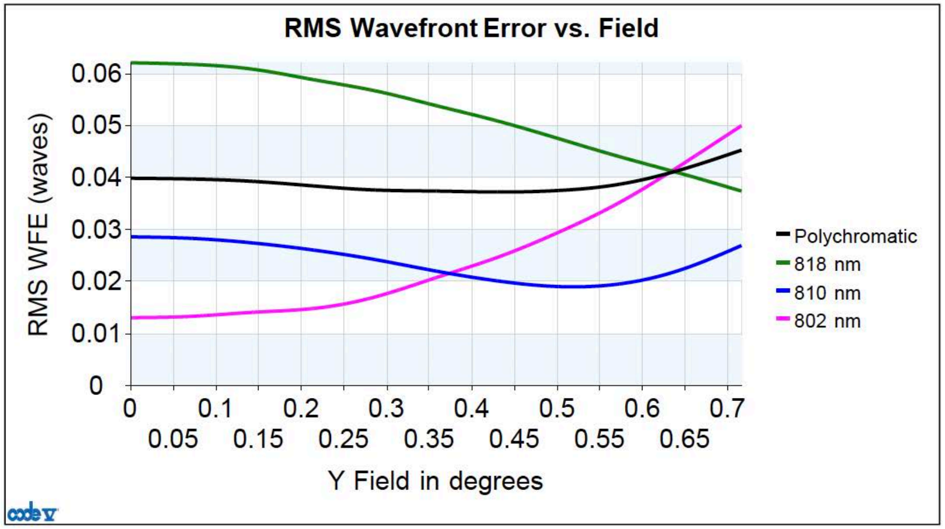
- SNR of quantum microscope is much higher than for classical microscope but decreases rapidly with transmission loss
- Design uses small number of elements (4) to achieve high throughput.



J. Li et al., Phys. Rev. A 97, 052127 (2018).

- Design is well corrected against wavefront aberrations.

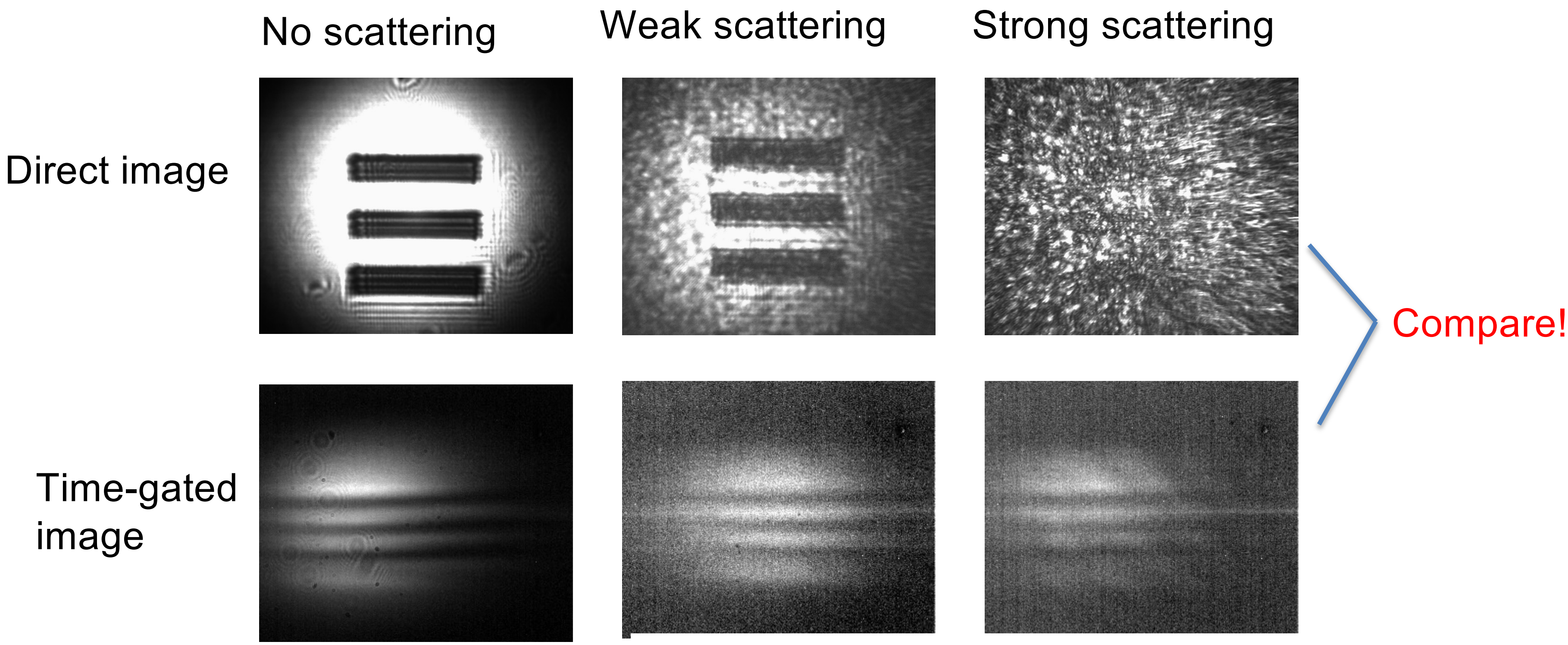




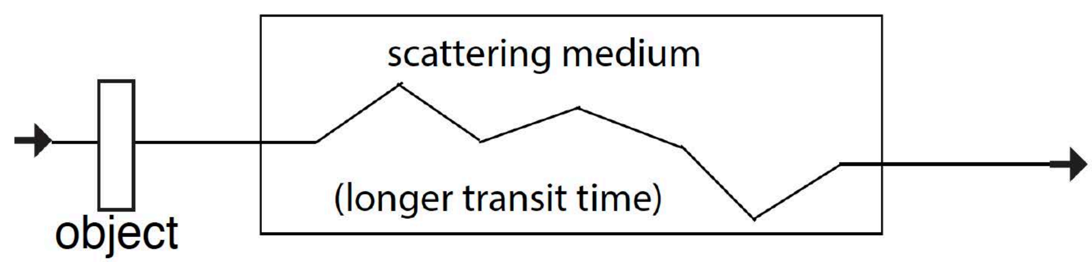
3. Imaging through a Strongly Scattering Medium

Imaging Through a Strongly Scattering Medium

We use time-gating to measure only the first-arriving photons



- Need a material with a strong, fast nonlinear optical response to construct time-gate.
- We use indium tin oxide (ITO), a transparent conducting oxide (TCO) with a strong, fast response.



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See also Wang et al (Alfano group) Science 253, 769 (1991),

Huge Nonlinear Optical Response of Indium Tim Oxide (ITO) at ENZ

- We need highly nonlinear, low-loss materials for switches and gates. (Ideally we want to be able to use weak control beams.)

- Note that optical nonlinearities are strongly enhanced at wavelengths for which n ≅ 0. (This is the ENZ, epsilon-near-zero, condition.)

$$n_2 = \frac{3\chi^{(3)}}{4\epsilon_0 c\, n_0\, \mathrm{Re}(n_0)}$$

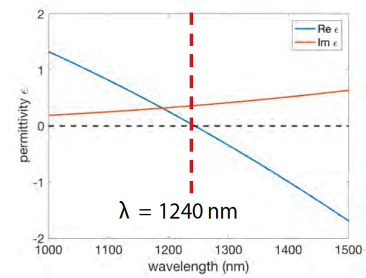
- Note further that for any conductor Re $\varepsilon = 0$ at the reduced plasma frequency :

$$\epsilon(\omega) = \epsilon_\infty - \frac{\omega_p^2}{\omega(\omega + i\gamma)}$$

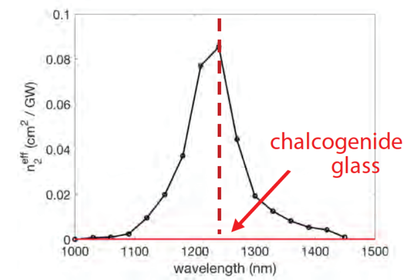
- For indium tin oxide (ITO), Re ε =0 at $\lambda = 1.24$ μm.

Characterization of ITO

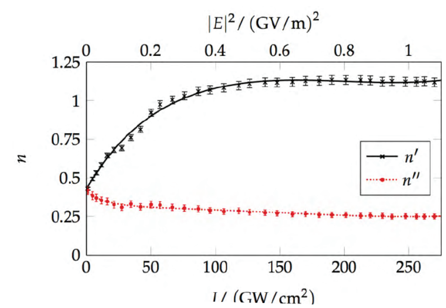
- ellipsometry



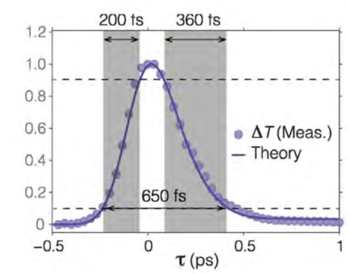
- n_2 can be 3.4 x10^5 times larger than that of silica glass



- overall change in refractive index of 0.8



- sub picosecond reponse time



M. Z. Alam et al., Science 352, 795-797 (2016)

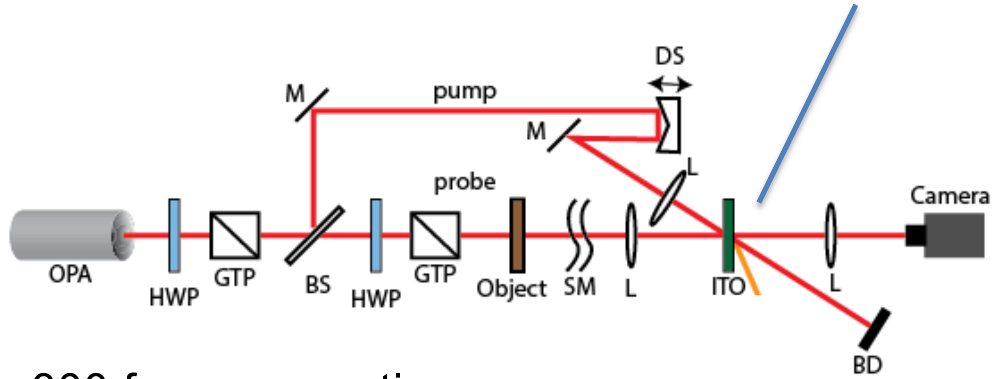
n_2 is approximately 300,000 times larger than that of silica glass

Experiment Setups

Nonlinear Transmission Setup

Uses a Kerr Gate
Similar to 1991 setup of Alfano

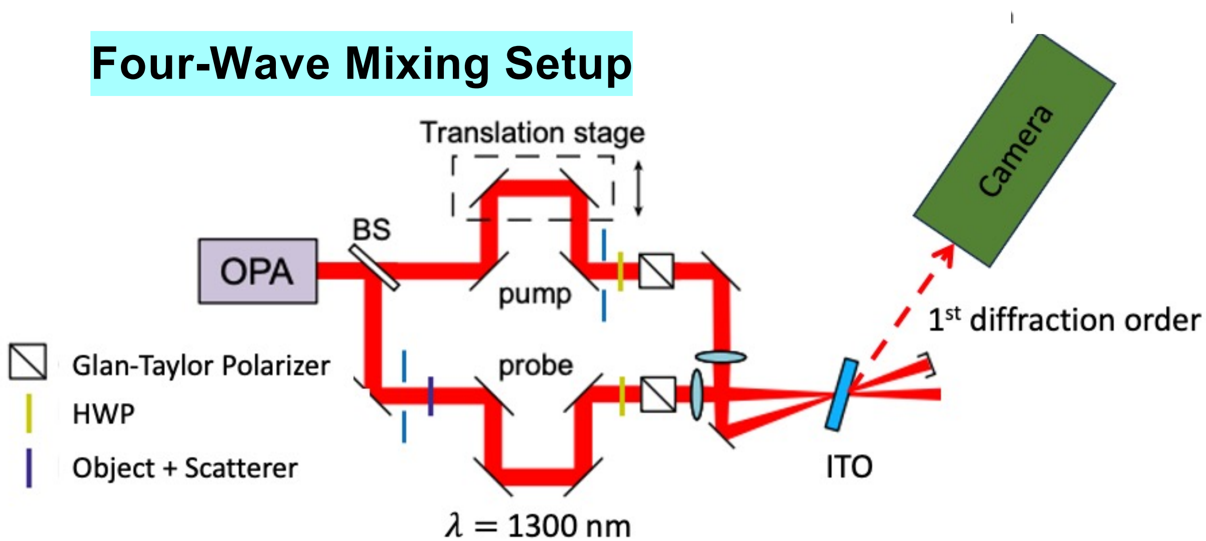
Probe transmission shuttered
by pump pulse in a “Kerr gate.”



GTP: Glan-Taylor polarizer
SM: scattering media
BS: beam splitter
BD: beam dump
DS: delay stage
L: lens
M: mirror

300 fs response time

Four-Wave Mixing Setup



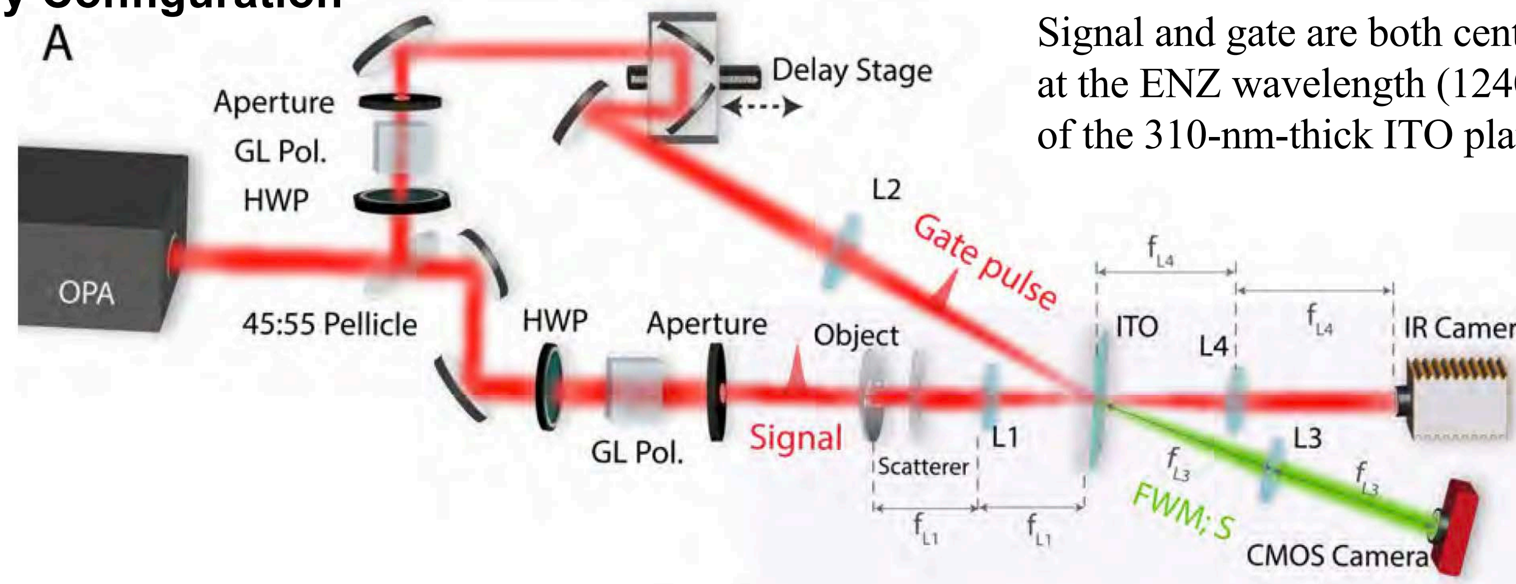
Pump and probe are both centered at the ENZ wavelength (1240 nm) of the 310-nm-thick ITO plate

120 fs response time

- We use the four-wave mixing setup because it gives a shorter gating time and suppresses background.

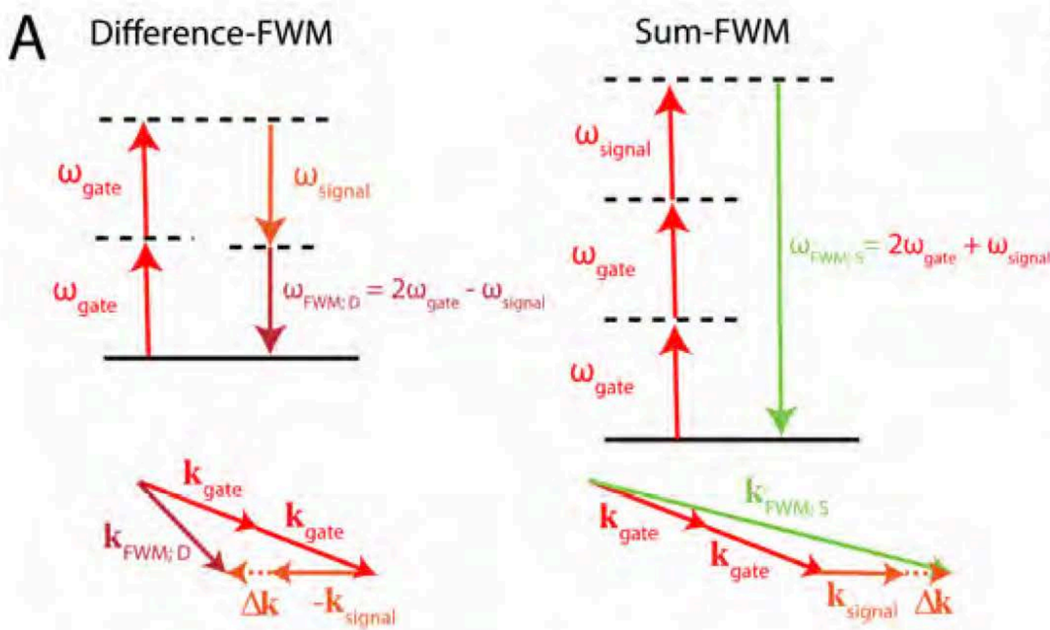
Four-Wave-Mixing Optical Time-Gating

Laboratory Configuration



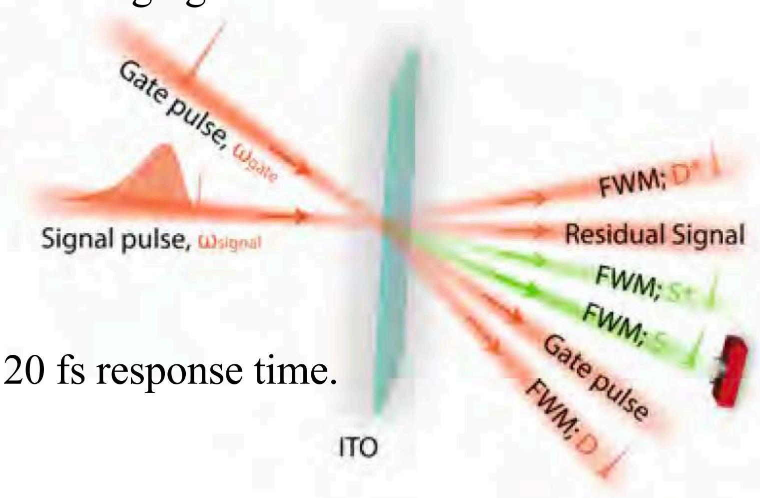
Signal and gate are both centered at the ENZ wavelength (1240 nm) of the 310-nm-thick ITO plate

Nonlinear Interaction



B

Sum four-wave mixing interaction shifts the signal from the IR to the visible where imaging detectors are more sensitive.



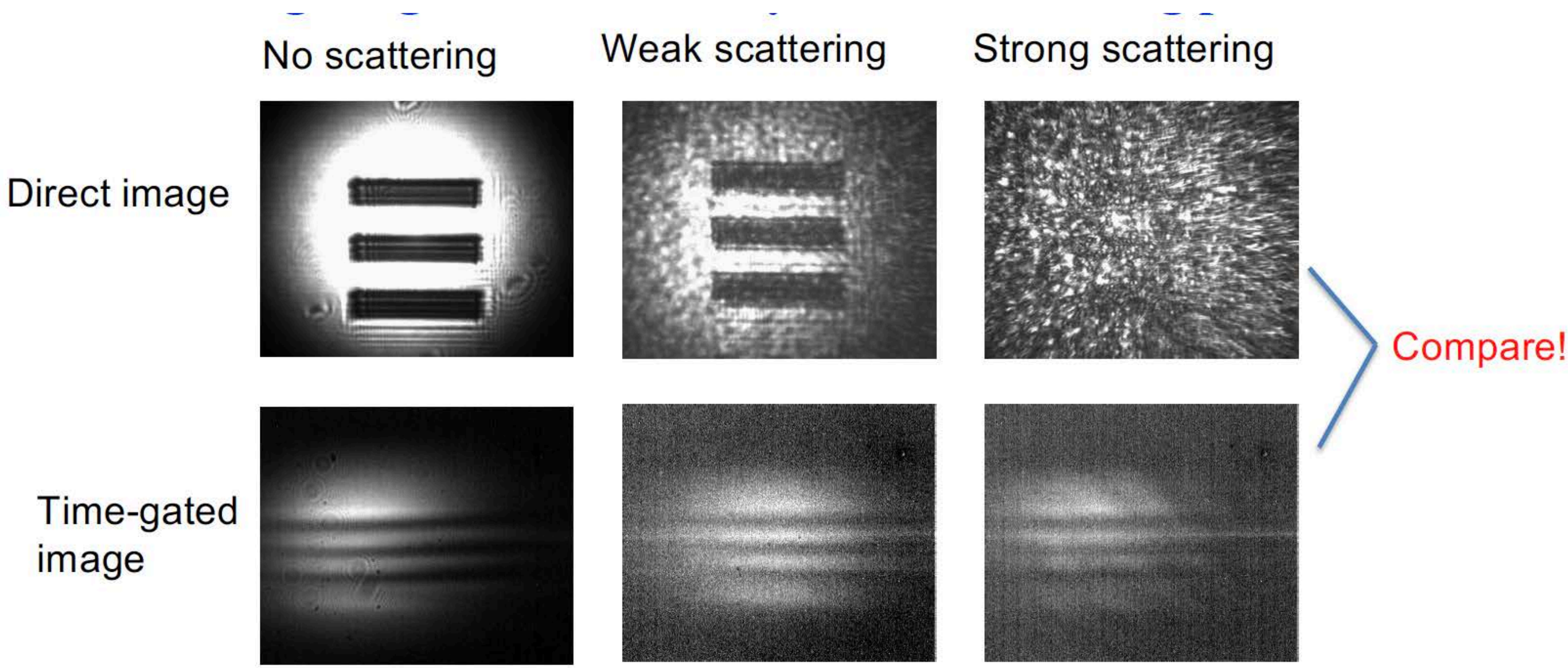
120 fs response time.

Summary: Imaging through a Strongly Scattering Medium

We have demonstrated an imaging method that
- Preserves the spatial resolution of the object
- Is background free
- Converts image to a desirable wavelength

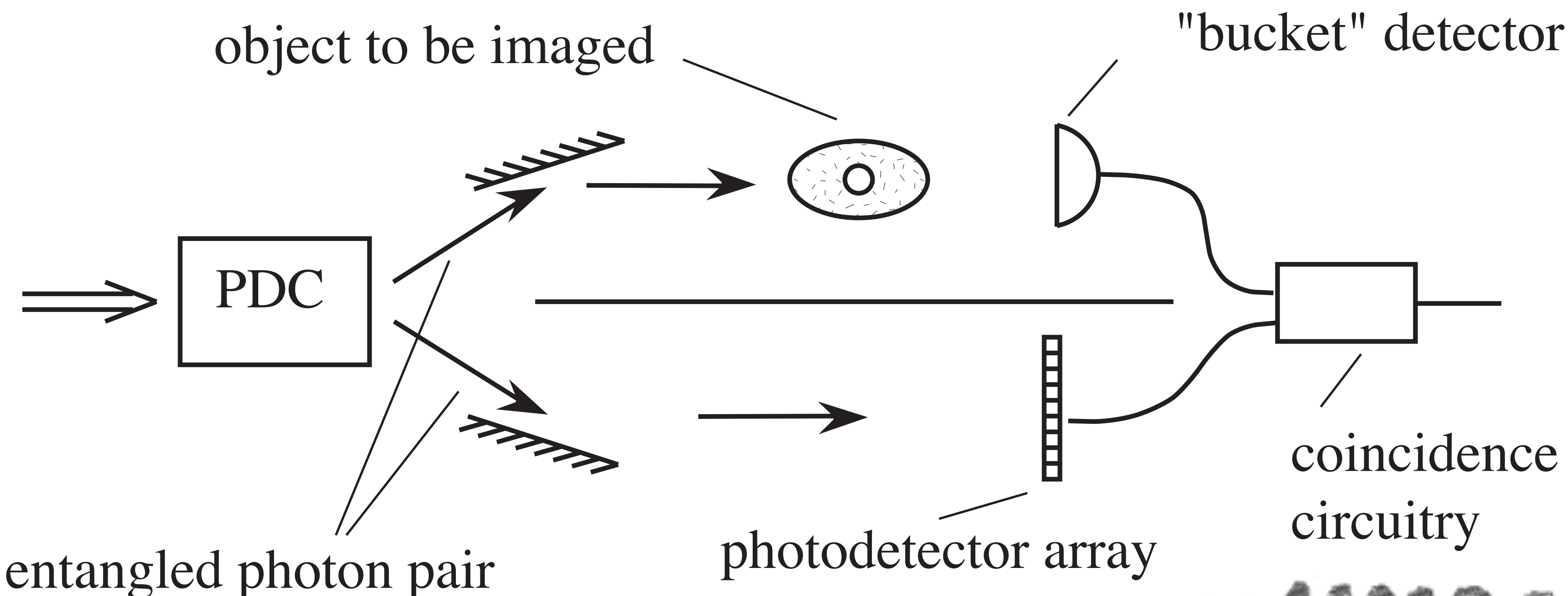
Our approach involves time-gating using a highly nonlinear ENZ material
- Time-gate transmits only the unscattered photons, which contain the image information

Useful for
- Non-invasive biomedical imaging and tomography
- Optical (including OAM-based optical) communication through atmospheric turbulence

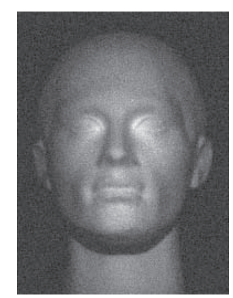


Interaction-Free and Ghost Imaging

Ghost (Coincidence) Imaging



- Obvious applicability to remote sensing!
  (imaging under adverse situations, bio, two-color, etc.)
- Is this a purely quantum mechanical process? (No)
- Can Brown-Twiss intensity correlations lead to ghost imaging? (Yes)



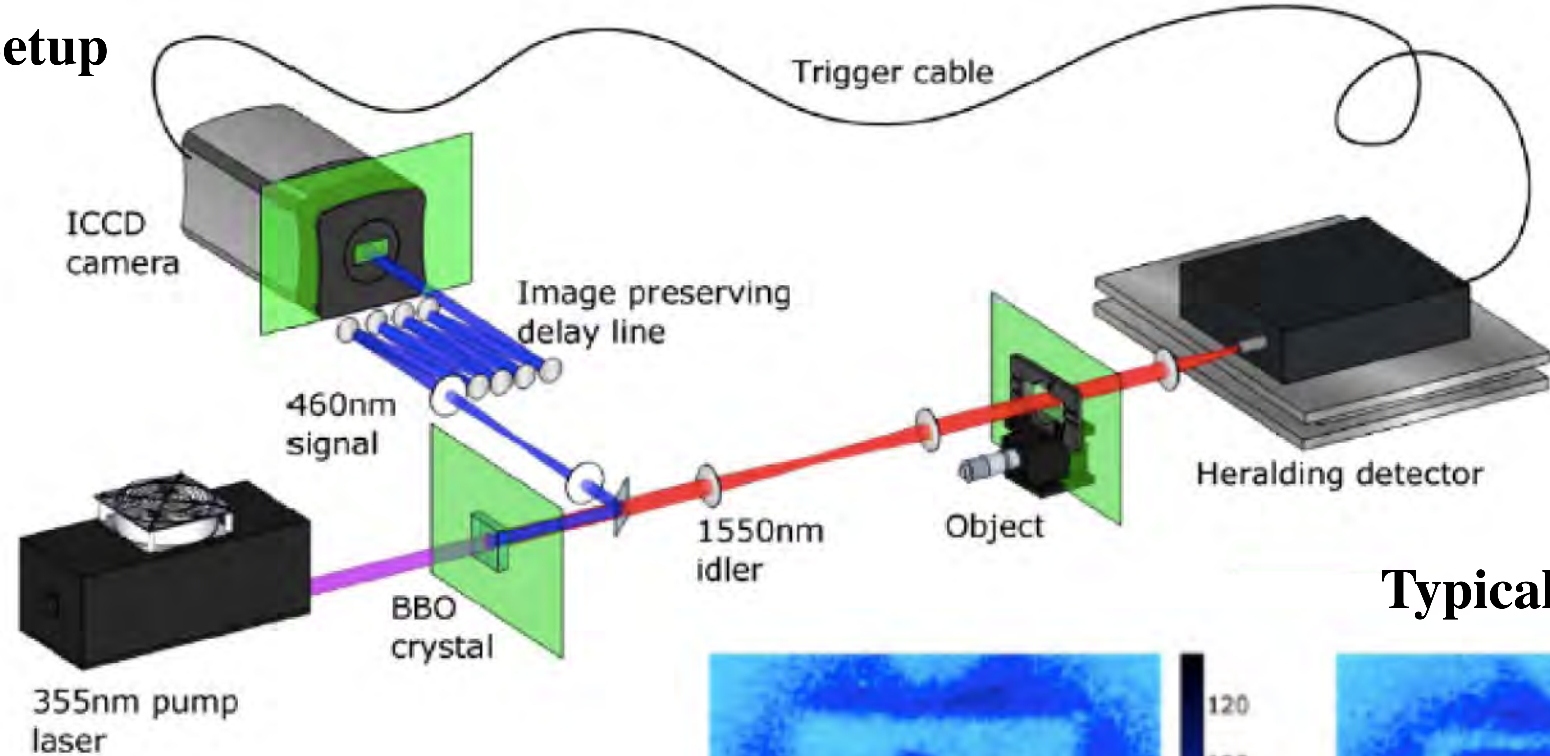
Padgett Group

Strekalov et al., Phys. Rev. Lett. 74, 3600 (1995).
Pittman et al., Phys. Rev. A 52 R3429 (1995).
Abouraddy et al., Phys. Rev. Lett. 87, 123602 (2001).
Bennink, Bentley, and Boyd, Phys. Rev. Lett. 89 113601 (2002).
Bennink, Bentley, Boyd, and Howell, PRL 92 033601 (2004)
Gatti, Brambilla, and Lugiato, PRL 90 133603 (2003)
Gatti, Brambilla, Bache, and Lugiato, PRL 93 093602 (2003)

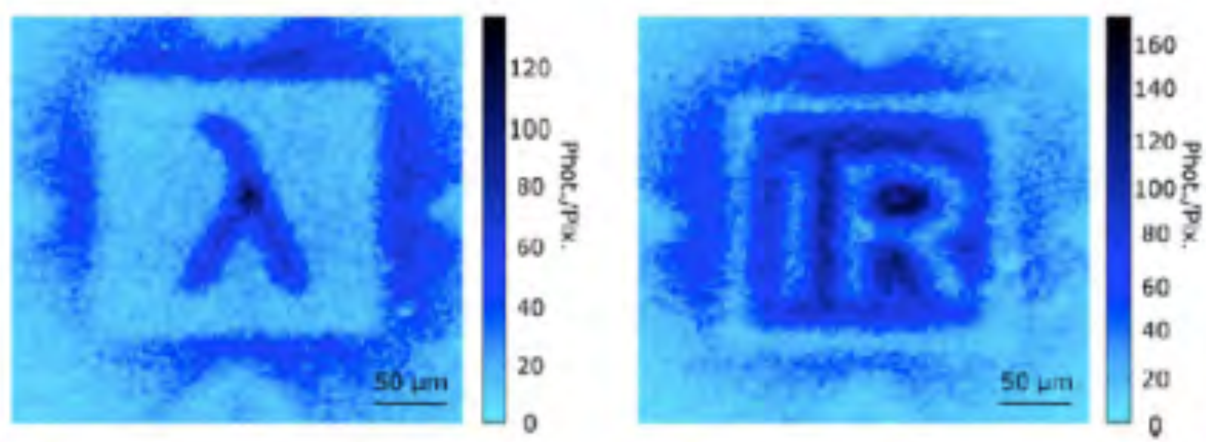
Wavelength-Shifted (Two-Color) Ghost Microscopy

- Pump at 355 nm produces signal at 460 nm and idler at 1550 nm
- Object is illuminated at 1550 nm, but image is formed (in coincidence) at 460 nm
- Wavelength ratio of 3.4 is the largest yet reported.

Setup

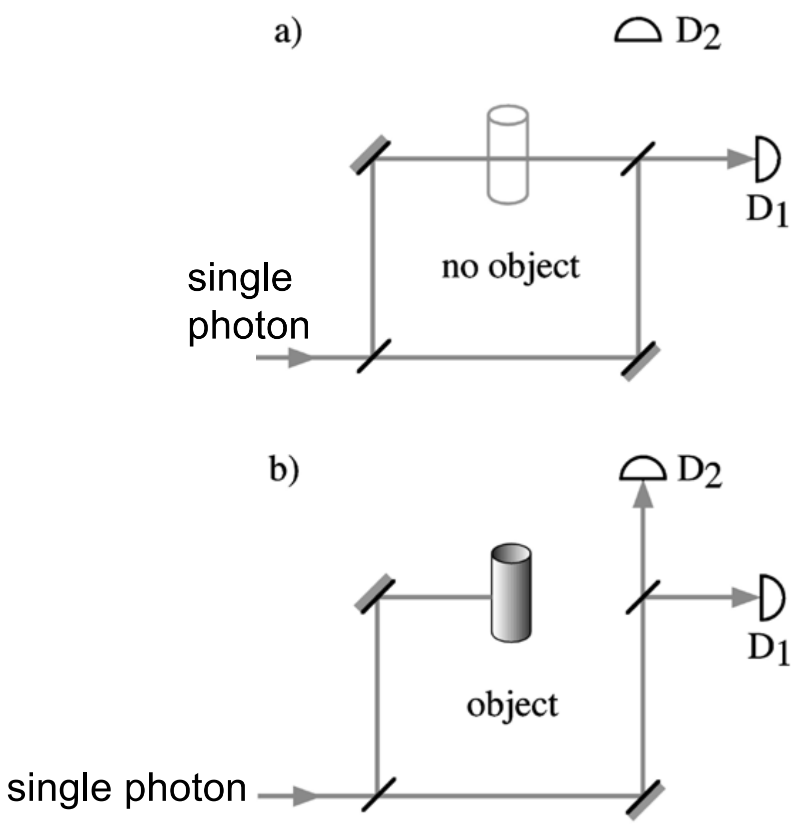


Typical images

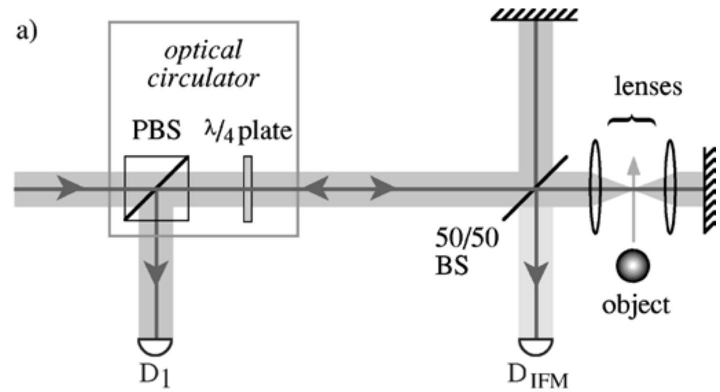


Photon-sparse microscopy: visible light imaging using infrared illumination, R.S. Aspden, N. R. Gemmell, P.A. Morris, D.S. Tasca, L. Mertens, M.G. Tanner, R. A. Kirkwood, A. Ruggeri, A. Tosi, R. W. Boyd, G.S. Buller, R.H. Hadfield, and M.J. Padgett, Optica 2, 1049 (2015).

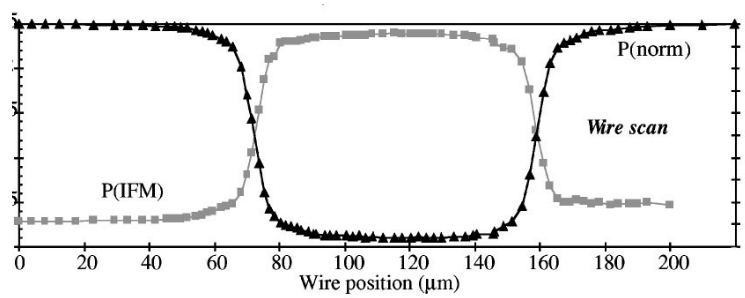
Quantum Imaging by Interaction-Free Measurement



imaging setup



results

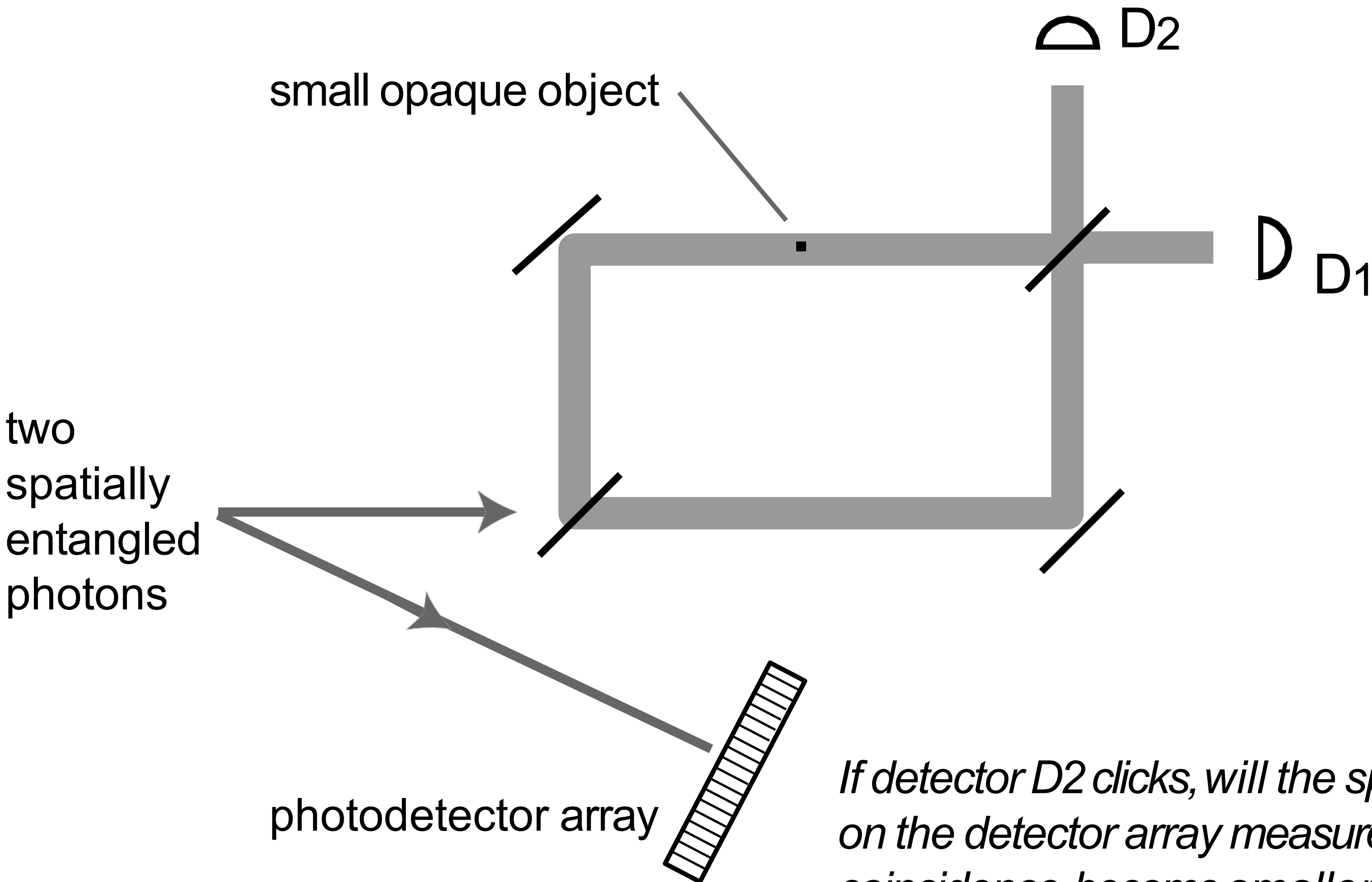


As shown, the object is detected by an interaction-free measurement (that is, D2 registers a photon) 25% of the time. There are other (Zeno) configurations that can lead to a 100% success rate.
Predicted by Elitzur and Vaidman and confirmed by White et al.

White et al. later showed that interaction-free measurements (IFMs) could be used in an imaging configuration to determine the diameter of a wire using only photons that did not physically interact with the wire.

A. Elitzur and L. Vaidman, Found. Phys. 23, 987 (1993).
L. Vaidman, Quant. Opt. 6, 119 (1994).
P. Kwiat, H. Weinfurter, T. Herzog, A. Zeilinger, and M. A. Kasevich, Phys. Rev. Lett. 74, 4763 (1995)
A. G. White, J. R. Mitchell, O. Nairz, and P. G. Kwiat, Phys. Rev. A 58, 605 (1998).

Interaction-Free Measurements and Entangled Photons



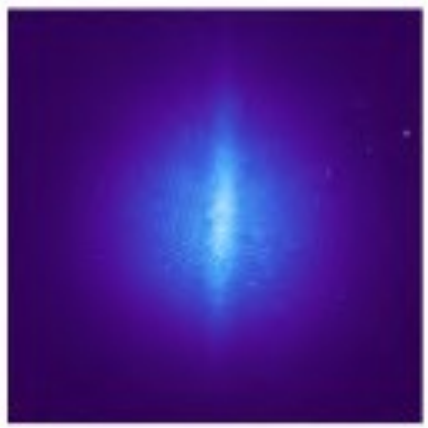
If detector D2 clicks, will the spot size on the detector array measured in coincidence become smaller?

- Does an interaction-free measurement constitute a "real" measurement?
- Does it lead to the collapse of the wavefunction of its entangled partner?
- More precisely, does the entire two-photon wavefunction collapse?

Laboratory Results

Interaction-free ghost image of a straight wire

coincidence counts



singles counts

- Note that the interaction-free ghost image is about five times narrower than full spot size on the ICCD camera

- This result shows that interaction-free measurements lead to wavefunction collapse, just like standard measurements.

Zhang, Sit, Bouchard, Larocque, Grenapin, Cohen, Elitzur, Harden, Boyd, and Karimi, Optics Express 27, 2212-2224 (2019).

Is interaction-free imaging useful?

Interaction-free imaging allows us to see what something looks like *in the dark*!

Could be extremely useful for biophysics, for example:

What does the retina of the eye look like when light does not hit it?

Similarly, what does the green alga Chlamydomonas reinhardtii (which is a common reference organism in the study of photosynthesis) look like when light does not hit it.

Research in Quantum Imaging

Quantum Imaging or Quantum Imogene?

Sid Caesar and Imogene Coca in 1953

Special Thanks To My Students and Postdocs!

Ottawa Group

Rochester Group