A new type of transmission and reflection microscopy, ‘ptychography,’ works by calculating the image of an object from the intensity of the scattered radiation, leading to a wide range of innovative applications.

When we think of a conventional transmission or reflection microscope, we think of lenses, particularly condenser, objective, and eye-piece lenses. However, we recently developed a form of computational microscopy—ptychography—1–3—that can operate with no lenses at all and is able to produce more informative images than those obtained with lenses (see Figure 1).

The data we record is the Fresnel or Fraunhofer diffraction pattern of the radiation that is scattered from an object (see Figure 2). To form an image using this information, we face a tricky mathematical problem: detectors can only measure the power that is delivered by an optical wave. But the times at which the peaks and troughs of these waves arrive at the detector (i.e., their relative phase) are completely lost. The problem is that nearly all useful structural and quantitative information about the specimen is encoded in the phase of the scattered wave field.

The defining characteristic of ptychography is that two or more diffraction patterns are recorded from overlapping areas of the specimen. This creates redundancy in the measured data, which allows a computer algorithm to solve for the lost phases very efficiently. At present, we can solve for a million unknown phases (i.e., the phases of every pixel in a 1k×1k pixel² camera) in less than half a second, and we have still not fully optimized the algorithm. Once we have retrieved all phases, we can computationally propagate the wave from the detector’s location back to the object plane.

At first sight, this might seem like a very complicated way of doing something that can be done very easily by a lens. However, ptychography has some unique advantages. Perhaps the most important of these is that the method produces two images. One corresponds to a map of how much the object has absorbed or scattered the light passing through it. The second represents the phase that has been introduced into the light. It is the quality, contrast, and quantitative nature of the second signal that is unique to ptychography. Many specimens of interest (say, biological cells) are essentially transparent, so that they produce no contrast at all in conventional, bright-field images. Biologists have developed ways of approximating this phase information, e.g., based on using a Zernike phase plate or differential phase contrast. But these methods, although referred to as ‘phase imaging,’ do not produce a quantitative phase map over...
Figure 2. Typical Fraunhofer (far-field) diffraction pattern scattered from a specimen, displayed on a logarithmic scale to enhance intensity at high scattering angles.

the entire field of view. Figure 3 shows the phase profile of a toric contact lens as an extreme example of the power of ptychography. The phase signal is directly proportional to the optical thickness of the lens. The field of view is 14mm (diameter), which is enormous by the standards of conventional imaging, but the phase image is accurately quantitative (with optical-thickness sensitivity of better than 0.1μm) and does not suffer from any artifacts. This is particularly useful for imaging cells (see Figure 4), where the phase image is exceptionally clean and has high contrast. In reflection mode (see Figure 5), we have measured phase changes of a fraction of 0.1% of π, corresponding to height variations of less than 1nm.

It would be wrong to suggest that there are no other interferometric techniques that can deliver surface-profile and/or wave-phase information. However, methods such as holography or white-light profilometry require exacting specifications on the physical stability of the measuring equipment. In contrast, because ptychography uses diffraction alone (i.e., the specimen itself is the interferometer), it is very insensitive to vibrations.

Because ptychography uses a computer-generated lens, it has some further distinct advantages. It can operate at extremely long working distances (5cm or more). As long as the detector subtends a suitably large effective numerical aperture in the specimen plane, it is possible to obtain high-resolution images through thick, sealed bottles, Petri dishes, etc. In addition, once the data has been collected, the user can retroactively refocus the computational lens, just like turning the focus knob on a conventional microscope. However, perhaps the most exciting application of ptychography—and a focus of our

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ongoing research—is in improving resolution and phase contrast in x-ray\(^4,5\) and electron microscopy,\(^6\) for which good-quality lenses cannot be manufactured.

Images and data were supplied by Martin Humphry, Andy Hurst, and Ian Pykett (Phase Focus Ltd.), as well as by Andrew Maiden (University of Sheffield).

**Figure 5.** Phase (color) and amplitude (hue) image of a semiconductor device seen in reflection mode. The phase is affected by both the height of the features and their dielectric constants.