Interferometric hard x-ray phase contrast imaging at 204 nm grating period

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We report on hard x-ray phase contrast imaging experiments using a grating interferometer of approximately 1/10th the grating period achieved in previous studies. We designed the gratings as a staircase array of multilayer stacks which are fabricated in a single thin film deposition process. We performed the experiments at 19 keV x-ray energy and 0.8 μm pixel resolution. The small grating period resulted in clear separation of different diffraction orders and multiple images on the detector. A slitted beam was used to remove overlap of the images from the different diffraction orders. The phase contrast images showed detailed features as small as 10 μm , and demonstrated the feasibility of high resolution x-ray phase contrast imaging with nanometer scale gratings. © 2013 American Institute of Physics. [<http://dx.doi.org/10.1063/1.4788910>]

I. INTRODUCTION

Hard x-ray phase contrast imaging using grating interferometers holds the potential for greatly improved image contrast when compared to absorption imaging.^{1–6} Recently there has been continuing successes in achieving ever smaller grating periods^{7–9} which are motivated by several beneficial factors. The first is that the amount of phase contrast increases with the diffraction angle of the grating, which is inversely related to the period of the grating. Even though very small grating periods necessitate interferometer designs outside the near field regime, a number of studies showed that far field interferometers can work as well under the right geometric configurations.^{10–13} Another motivation for smaller grating periods is the image resolution. Recently, a number of promising approaches have been developed in x-ray microscopy that utilizes gratings to extract phase contrast.^{14–16} In interferometry-based imaging, an individual pixel of the image should span several interference fringes in order for the phase shift measurement to be well defined for the pixel. As a result, high resolution imaging benefits from small grating periods.

However, sub-micron periods for hard x-ray gratings are difficult to realize with conventional micro-fabrication techniques, due to the grating thickness required for x-ray intensity modulation at these energies. The combination of small periods and large thicknesses proved to be a significant challenge for the etching processes in conventional fabrication procedures. Therefore, hard x-ray imaging experiments up to date have not reached grating periods below 2.0 μm to our knowledge. In this study, we performed phase contrast imaging experiments at the fringe period of 204 nm and 19 keV photon energy using gratings of a novel multilayer array design, which were fabricated by an alternative thin film depo-

sition process. The experiments were carried out on a synchrotron beam line. The results showed the feasibility of an x-ray Talbot interferometer of ultra small grating periods as a high resolution imaging device.

II. DESIGN, FABRICATION, AND CHARACTERIZATION OF GRATINGS

We developed a multilayer array design for hard x-ray gratings and fabricated absorption gratings of 204 nm period for the 17.5–25 keV energy range.¹⁷ The multilayer array design extends the idea of Kim *et al.* using a multilayer stack as a transmission grating¹⁸ and allows us to realize very small grating periods over areas of several centimeters through a thin film deposition process. The grating design and fabrication method has been described in detail previously.¹⁷ Illustrated in Fig. 1(a), multiple bi-layers of tungsten (W) and silicon (Si) were deposited onto a staircase substrate to form an array of multilayer stacks. Each stack works as a micro grating. The substrate was fabricated from a 28° off-cut silicon wafer by UV lithography and anisotropic etching.¹⁷ It had a step height of 4.69 μm and a step width of 10 μm . A total of 46 individual layers of alternating W/Si, each one 102 nm thick, were then deposited to build up multilayer stacks of 4.69 μm total height, matching the height of a staircase step. The period of the grating is equal to the bi-layer thickness of 204 nm. With shadowing effects from the overhang of the substrate step edges during the deposition process, the width of the multilayer stack was 7.5 μm , which is effectively the depth of the grating. A polymer layer (SU8) of several microns was then spin coated onto the top of the multi layers as a protective cover.

The gratings were evaluated by slit diffraction experiments on a synchrotron beam line (2-BM beam line, Advanced Photon Source, Argonne National Laboratory,

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FIG. 1. Design and testing of absorption gratings. (a) The grating consists of an array of stacks of alternating layers of tungsten and silicon, which are deposited on a staircase silicon substrate in a single deposition process. The grating period is the thickness of a W/Si bi-layer, which is 204 nm. The width of the stacks is $7.5\ \mu\text{m}$. The height of the stacks is $4.7\ \mu\text{m}$ and matches that of the steps of the staircase. The incoming x-ray beam illuminates the multilayer stacks laterally. The intensity profile of the diffracted beams at the x-ray energy of 19 keV is plotted on the right, and shows that the grating efficiently diffracts energy into the ± 1 and higher order side bands. (b) The intensity modulation by the grating at 19 keV was directly imaged with a contact lithography method, in which the transmitted beam imprints a relief profile on the surface of an electron-beam resist polymer layer. Atomic force microscopy of the polymer surface profile is shown on the left, and the height profile is plotted on the right.

USA). The diffraction profile at 19 keV is illustrated in Fig. 1(a). It can be seen that the grating efficiently diffracts energy into the ± 1 and higher diffraction orders.

To visualize directly the x-ray intensity modulation by the gratings, we imaged the transmitted intensity of the x-ray beam through the grating by a contact radiography method. The method is modified from that described by Kim *et al.*¹⁸ and will be reported in detail in a separate manuscript. Briefly, a custom high resolution radiography film was placed in contact with the grating, which was exposed to the transmitted x-ray beam. The film consisted of a 10 nm gold layer over a 100 nm layer of electron-beam resist polymer. X-ray beam impacts the gold layer and exposes the polymer layer to secondary electrons. The polymer layer was chemically developed so that the surface profile becomes a relief image of the beam intensity. The surface profile was imaged with atomic-force microscopy (AFM). As illustrated in Fig. 1(b), the AFM image shows the periodic intensity modulation of the transmitted x-ray beam by the grating.

III. ASSEMBLY OF THE IMAGING SYSTEM

With the multilayer array gratings we constructed an interferometer in the form of two nominally identical, parallel gratings separated by the Talbot self-imaging distance of 0.7 mm, as illustrated in Fig. 2. Due to the 28° inclination angle of the grating staircase substrate, the incident x-ray beam is at a 62° angle from the normal direction of the grating surfaces. We have previously shown that an oblique incidence interferometer has its equivalent normal incidence configuration,¹⁹ such that the Talbot self-imaging phenomenon still applies. In our two grating setup, the image of the first grating falls onto the second grating, which acts as the analyzer.³ The exit beam is diffracted into multiple orders and propagates over a distance of 65.5 cm before reaching the x-ray detector. Each diffraction order contains an image of the sample. On the scintillator screen of the detector, the lateral separation of adjacent diffraction orders was observed to be $200\ \mu\text{m}$. To avoid overlap of the images from the different

FIG. 2. Setup and operation of the imaging system. The 19 keV x-ray beam is narrowed by a tungsten slit of $200\ \mu\text{m}$ width before illuminating the sample. The transmitted beam passes through the interferometer, which consists of two parallel gratings separated by one Talbot distance. The interferometer diffracts the beam into multiple bands, each containing an image of the sample. The distance between the interferometer and the detector allows complete separation of the diffraction bands and prevents overlap of the multiple images. Phase stepping is realized by tilting the stage of the interferometer at 0.001° increments.

diffraction orders, a slit of $200\ \mu\text{m}$ height was placed in front of the imaged object.

Imaging experiments with the interferometer were performed on the 2-BM beam line of Advanced Photon Source (APS), Argonne National Laboratory, USA. The beam line was configured as a monochromatic parallel beam of 19 keV energy, with a vertical beam divergence of $1.9\ \mu\text{rad}$. The detector matrix was 2046×2046 pixels and the effective pixel size was $0.8\ \mu\text{m}$. The two gratings were set to be slightly non-parallel, such that the interference fringes from the first grating were masked by the second grating to form broad moiré fringes that could be directly resolved by the detector (Fig. 3).

Experimentally, we found that both the moiré fringe pattern and the average intensity in each diffraction band on the detector plane were highly depended on the incident angle of the beam. They fluctuated in a complex way when the incident angle was varied. This can be understood from the point of view that the wave amplitude in the q th diffraction band on the detector is the sum of a number of diffraction pathways. Each pathway undergoes an m th order diffraction through the first grating and an n th order diffraction through the second grating such that $m + n = q$. The diffraction amplitudes of the gratings vary in both magnitude and phase with the incident angle of the beam. Consequently, the amplitudes and relative

phases of the diffraction pathways that sum up to the wave amplitude in a diffraction band also vary with the incident angle, resulting in the complex fluctuations of the moiré fringe pattern and intensity. Additionally, at certain incident angles the staircase substrate of the gratings introduced modulations of the diffracted beams, which lead to broad modulations of the moiré fringes. Taking all of these into account, the search for the optimal incident angle was based on several criteria. These included optimization of the fringe visibility in the central brightest diffraction band, while maintaining its intensity and avoiding the broad substrate level modulation. An example of an optimal condition is shown in Fig. 3. Here strong moiré fringes are visible in the even diffraction orders, including the central 0th and ± 2 side bands. Horizontal lines of $4.7\ \mu\text{m}$ spacing can also be seen and arise from the slight mismatch between the multilayer stacks on adjacent steps of the staircase substrate.

IV. IMAGE PROCESSING

To quantify the phase shift of the interference fringes, it is necessary to perform the phase stepping procedure, where one grating is displaced relative to the other in the lateral direction perpendicular to the grating lines, and the periodic fluctuation of the transmitted intensity is recorded.⁵ In our case the interferometer was just a few centimeters in size and fitted on a single motorized stage. Thus for phase stepping, instead of independently moving one grating relative to the other, the whole interferometer was tilted around the transverse horizontal axis at 0.001° increments. The rotation effected vertical displacements of 12 nm per step between the two gratings. This resulted in “traveling” moiré fringes shown in Fig. 3 and a movie (cf. Video 1) is available online. The intensity fluctuations at fixed points on the detector as a function of the phase stepping movement are plotted in Fig. 3 for the 0th and ± 2 diffractions bands. The fringe visibility, defined through the pixel intensity as $(I_{\text{max}} - I_{\text{min}})/(2 I_{\text{mean}})$, was 53% for the central 0th diffraction order, and 46% for the ± 2 diffraction orders.

FIG. 3. Intensity oscillation from phase stepping scans. Referring to the imaging setup in Fig. 2, the image on the detector contains a number of separate diffraction bands which are labeled on the left of the image. The visible vertical fringes in the bands are moiré fringes arising from a slight rotation of one grating relative to the other, while the underlying 204 nm interference fringes are below the resolution of the detector. The even order diffraction bands have stronger fringes. During phase stepping, the moiré fringes travel, and the intensity fluctuation of fixed pixels in the 0th and ± 2 diffraction bands are plotted on the right. The fringe visibility was 53% for the 0th and 46% for the ± 2 diffraction bands. The fringe patterns in the ± 1 bands contain a broad modulation attributable to the staircase substrate of the gratings. The fringe visibility in these bands ranged from 13.5% to 31% (enhanced online) [URL: <http://dx.doi.org/10.1063/1.4788910.1>].

Three types of images including absorption, differential phase contrast, and dark field were obtained from a set of phase stepped images. Image processing is based on the assumption that the number of acquired steps in a phase stepping cycle is sufficient to capture the shape of the phase stepping curve, i.e., to sample all the significant Fourier components in the curve. This is borne out by the data shown in Fig. 3. The complex amplitude of the interference fringe at each pixel was calculated as the amplitude of the intensity fluctuation at the period of the phase stepping curve, noted as N , by the formula,

$$A_1(x, y) = \frac{1}{N} \sum_{n=1}^N I_n(x, y) e^{-i2\pi n/N}, \quad (1)$$

where $I_n(x, y)$ is the intensity at pixel coordinates (x, y) in the n th phase step. To account for imperfections in the gratings, a calibration data set was measured without any sample. Noting the calibration image intensity and fringe amplitude as I_n' and A_1' , the differential phase contrast image is given by

$$\varphi(x, y) = \text{phase}[A_1(x, y)/A_1'(x, y)]. \quad (2)$$

The dark field image is the attenuation of the fringe amplitude relative to that of the mean intensity,^{20,21}

$$F_D(x, y) = -\ln[A_1(x, y)/A_1'(x, y)] + \ln[\langle I_n(x, y) \rangle / \langle I_n'(x, y) \rangle]. \quad (3)$$

The absorption image is simply the attenuation of the mean intensity relative to the calibration value,

$$F_A(x, y) = -\ln[\langle I_n(x, y) \rangle / \langle I_n'(x, y) \rangle]. \quad (4)$$

V. RESULTS

The differential phase contrast image of a sample containing polystyrene spheres is shown in Fig. 4. Images of the spheres are replicated in each diffraction band of the interferometer. The even diffraction bands are less affected by artifacts arising from imperfections in the gratings, and generally provide better visualization of the spheres. This is consistent with the result shown in Fig. 3, where the even diffraction orders contain the strongest interference fringes.

FIG. 4. A phase contrast image of polystyrene beads showing multiple repeating images from different diffraction bands. The diffraction orders are labeled on the left. The image is extracted from a set of phase stepped images by quantifying the phase shift of the periodic intensity fluctuation at each pixel location. The even diffraction bands highlighted in white are less affected by imperfections in the gratings due to their stronger diffraction fringes (Fig. 3).

FIG. 5. Differential phase contrast, dark field, and absorption images of a portion of a fruit fly's head. These are extracted from the central 0th order diffraction band by the phase stepping procedure illustrated in Fig. 3. Details on the scale of $10 \mu\text{m}$, such as structures of the antenna (blue arrow) and units of the compound eye (green arrow), are most clearly seen in the differential phase image. In the absorption image, sharp edges are accentuated by Fresnel diffraction effects over the distance between the sample and the detector.

Due to the long distance between the second grating and the image detector, Fresnel diffraction at the lateral edges of the spheres resulted in horizontal displacement of the vertical moiré fringes, which lead to phase contrast at these locations that could not have been detected by the horizontal gratings. This can be seen in Fig. 4. Thus the Fresnel diffraction introduced phase contrast from gradients of refractive index in the horizontal direction, in addition to the phase sensitivity of the gratings towards refractions in the vertical direction.

The phase contrast, dark field, and absorption images of the head of a fruit fly are shown in Fig. 5. All three images were from the central 0th order diffraction band. The anatomical structures are most clearly seen in the differential phase contrast image, in particular the details of the compound eye and the antenna to the left of the eye. Features of $10 \mu\text{m}$ scale, such as hairs on the antenna and the individual units of the compound eye, are resolved in the phase contrast image. Additionally, detailed segment-like features of the antenna can only be seen in the differential phase contrast image. Due to the long distance between the interferometer and the detector, the absorption image is also enhanced by edge diffraction effects over this distance.²²

VI. CONCLUSION AND DISCUSSION

In this study we demonstrated phase contrast imaging experiments with an oblique-incidence Talbot interferometer at 204 nm grating period and 19 keV energy. The gratings are of a multilayer array design and are fabricated by a thin film deposition process on a staircase substrate. The small grating period resulted in several interesting characteristics. The first is the complete separation of multiple images from the different diffraction orders. Second, the compact size of the interferometer allowed it to be fitted on a single motorized stage.

Although the pixel size of the camera was $0.8 \mu\text{m}$, the actual resolution of the images was near $10 \mu\text{m}$. The broadening of the resolution can be explained by two factors. The

first is the angular divergence of the synchrotron beam, which is 6 μrad in the lateral direction and 2 μrad in the vertical direction. Based on the distance between the sample and the camera, the corresponding image blurring would be about 5 μm in the lateral direction. The second factor is the width of the photon burst in the scintillator crystal that converts x-ray to visible light, which was over 25 μm thick. Despite these factors, the grating periods are sufficiently small to support sub-micron image resolution for future phase-contrast imaging systems.

In the current experiments, the size of the synchrotron x-ray beam is a few millimeters, which is a fraction of the centimeter-sized gratings. Additionally, this first trial is based on a two-grating Talbot interferometer with one Talbot distance between the gratings. The short inter-grating distance resulted in phase contrast levels that are comparable to three-grating interferometers of longer distances and larger grating periods. A future focus will be the construction a Talbot-Lau interferometer which includes an additional absorption grating to modulate the x-ray source,⁶ thus allowing longer inter-grating distances and the potential to work with compact, cone-beam sources to provide larger field of views.

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- ¹J. F. Clauser, U.S. patent 5,812,629 (22 October 1998).
- ²P. Cloetens, J. P. Guigay, C. DeMartino, J. Baruchel, and M. Schlenker, *Opt. Lett.* **22**(14), 1059 (1997).
- ³C. David, B. Nohammer, H. H. Solak, and E. Ziegler, *Appl. Phys. Lett.* **81**(17), 3287 (2002).
- ⁴A. Momose, *Opt. Express* **11**(19), 2303 (2003).
- ⁵T. Weitkamp, A. Diaz, C. David, F. Pfeiffer, M. Stampanoni, P. Cloetens, and E. Ziegler, *Opt. Express* **13**(16), 6296 (2005).
- ⁶F. Pfeiffer, T. Weitkamp, O. Bunk, and C. David, *Nat. Phys.* **2**(4), 258 (2006).
- ⁷C. David, J. Bruder, T. Rohbeck, C. Grunzweig, C. Kottler, A. Diaz, O. Bunk, and F. Pfeiffer, *Microelectron. Eng.* **84**(5-8), 1172 (2007).
- ⁸D. Noda, M. Tanaka, K. Shimada, W. Yashiro, A. Momose, and T. Hattori, *Microsyst. Technol.* **14**(9-11), 1311 (2008).
- ⁹E. Reznikova, J. Mohr, M. Boerner, V. Nazmov, and P. J. Jakobs, *Microsyst. Technol.* **14**(9-11), 1683 (2008).
- ¹⁰U. Bonse and M. Hart, *Appl. Phys. Lett.* **6**(8), 155 (1965).
- ¹¹B. J. Chang, R. Alferness, and E. N. Leith, *Appl. Opt.* **14**(7), 1592 (1975).
- ¹²C. K. Kemble, J. Auxier, S. K. Lynch, E. E. Bennett, N. Y. Morgan, and H. Wen, *Opt. Express* **18**(26), 27481 (2010).
- ¹³J. Rizzi, T. Weitkamp, N. Guerinneau, M. Idir, P. Mercere, G. Druart, G. Vincent, P. da Silva, and J. Primot, *Opt. Lett.* **36**(8), 1398 (2011).
- ¹⁴Y. Takeda, W. Yashiro, Y. Suzuki, S. Aoki, T. Hattori, and A. Momose, *Jpn. J. Appl. Phys., Part 2* **46**(1-3), L89-L91 (2007).
- ¹⁵Y. Takeda, W. Yashiro, T. Hattori, A. Takeuchi, Y. Suzuki, and A. Momose, *Appl. Phys. Express* **1**(11), 117002 (2008).
- ¹⁶W. Yashiro, Y. Takeda, A. Takeuchi, Y. Suzuki, and A. Momose, *Phys. Rev. Lett.* **103**(18), 180801 (2009).
- ¹⁷S. K. Lynch, C. Liu, N. Y. Morgan, X. Xiao, A. A. Gomella, D. Mazilu, E. E. Bennett, L. Assoufid, F. de Carlo, and H. Wen, *J. Micromech. Microeng.* **22**(10), 105007 (2012).
- ¹⁸J. M. Kim, I. H. Cho, S. Y. Lee, H. C. Kang, R. Conley, C. Liu, A. T. Macrander, and D. Y. Noh, *Opt. Express* **18**(24), 24975 (2010).
- ¹⁹H. Wen, C. K. Kemble, and E. E. Bennett, *Opt. Express* **19**(25), 25093 (2011).
- ²⁰F. Pfeiffer, M. Bech, O. Bunk, P. Kraft, E. F. Eikenberry, C. Bronnimann, C. Grunzweig, and C. David, *Nature Mater.* **7**(2), 134 (2008).
- ²¹H. Wen, E. Bennett, M. M. Hegedus, and S. C. Carroll, *IEEE Trans. Med. Imaging* **27**(8), 997 (2008).
- ²²S. W. Wilkins, T. E. Gureyev, D. Gao, A. Pogany, and A. W. Stevenson, *Nature (London)* **384**(6607), 335 (1996).