Multi-modal hard x-ray imaging with a laboratory source using selective reflection from a mirror

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Abstract: Multi-modal hard x-ray imaging sensitive to absorption, refraction, phase and scattering contrast is demonstrated using a simple setup implemented with a laboratory source. The method is based on selective reflection at the edge of a mirror, aligned to partially reflect a pencil x-ray beam after its interaction with a sample. Quantitative scattering contrast from a test sample is experimentally demonstrated using this method. Multi-modal imaging of a house fly (Musca domestica) is shown as proof of principle of the technique for biological samples.

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1. Introduction

Multi-modal imaging is the ability to detect, within a single measurement, multiple types of contrast. For x-ray imaging several sources of contrast arise from different mechanisms of interaction of x-rays with matter [1]. Restricting our attention to elastic processes only, the predominant interaction mechanisms generating imaging contrast are photoelectric absorption and elastic scattering. These processes are responsible for absorption and phase contrast respectively [1]. For decades absorption contrast has been the chief method employed in x-ray medical imaging and non-destructive testing. On the other hand light materials, such as soft tissues, display poor absorption contrast and cannot in general be reliably measured with this method. Phase contrast is a means to overcome such limitations.

After the pioneering development of the x-ray interferometer due to Bonse and Hart [2], a multitude of phase-sensitive methods has been developed based on free space propagation [3], crystal interferometry [4], crystal analyzers [5, 6], grating interferometers [7, 8] and coded apertures [9].

An additional imaging modality, sensitive to ultra-small angle scattering, has been demonstrated using analyzer crystals [10], grating interferometers [11] and coded apertures [12]. Ultra-small angle scattering originates from the elastic interaction of x-rays with sub-micron structures within a sample. While imaging systems are generally not able to resolve sub-micron features individually, the previously mentioned scatter imaging modalities are very useful to distinguish regions within the sample where such features are present by looking at the overall scattering originated therein. The scatter imaging modality is often referred to as “dark field” imaging. In this paper we use the terms “dark field” and “scatter” imaging as synonyms and the combination of absorption, phase and scattering contrast in a single measurement is what we here term “multi-modal” imaging.

The wealth of information originating from multi-modal imaging can be a significant tool in bio-medical research [13–15]. Importantly, an increasing number of studies focus on the use of phase and scattering contrast with x-ray laboratory sources (see for instance [9, 12, 16–18]). This is a crucial step to ensure the applicability of multi-modal x-ray imaging methods in biological settings.

In this context we propose and experimentally demonstrate a novel multi-modal imaging method that is well suited to laboratory x-ray systems. The method is based on the selective reflection of x-rays at the edge of a mirror aligned below the critical angle for total reflection. Recently we have demonstrated quantitative phase imaging using this technique [18]. In this manuscript we demonstrate that, with a similar approach, scattering contrast can also be detected, in the same measurement, along with both absorption and phase information.
Fig. 1. Schematic of the experimental setup (not to scale). X-rays, after interacting with the sample, illuminate the mirror edge, aligned to partially obscure a given pixel row of the detector (I$_d$). Photons that strike the mirror are reflected onto a different pixel row (I$_r$). Weak scattering occurring at the sample may be detected around the direct beam direction, especially in a pixel row that is covered by the mirror shadow (I$_s$), generating a dark field image. For the data shown in this paper we used $z_1 = 100$ mm and $z_2 = 210$ mm. The mirror tilt angle was 3.3 mrad from the optic axis producing a transverse displacement of the reflected beam of about 1.5 mm at the detector position.

The paper is organized as follows: in Sec. 2 we review the principle of the measurement technique and describe the physical basis of the scattering contrast to which this technique is sensitive. In Sec. 3 the experimental results are presented and discussed. First we use a test sample to demonstrate that our method is capable of quantitative x-ray dark field imaging. Then we demonstrate the measurement of a biological specimen (a house fly) as an example of possible applications and the results are discussed. Finally the conclusions are drawn in Sec. 4.

2. Reflective edge illumination

The reflective edge illumination (REI) technique is inspired by the concept of edge illumination [19] where an x-ray pencil beam illuminates the edge of a single pixel of a detector. When a sample is scanned across such a beam, small refraction deviations are readily measured via intensity variations in the partially illuminated pixel. Appropriate combination of two images taken with edges aligned in opposite directions then enables quantitative phase and absorption imaging [17]. Moreover when the pencil beam is directed completely outside the measured pixel (such that no counts other than background can be detected), the presence of the sample may produce scattered photons directed to the “dark” pixel, efficiently realizing dark-field imaging [19] based on scattering contrast.

The REI method [18] utilizes a reflective edge instead of an absorbing one. In practice a mirror edge is aligned to partially obscure a pixel row in the detector, as depicted in Fig. 1. The photons that strike the mirror are directed onto a different row of pixels. When the sample is scanned across the beam, refraction deviations cause relative variations of the intensity of the direct (I$_d$) and reflected beam (I$_r$). As shown in [18], this mechanism enables quantitative phase and absorption imaging in a single scan.

In a similar way, a pixel that is totally obscured by the mirror (denoted by I$_s$ in Fig. 1), may detect scattered photons when the sample is scanned across the beam. Thereby genuine multi-modal imaging is accomplished in a single scan, where absorption, phase and dark-field images are simultaneously collected.

The interaction of x-rays with matter is well described by the (macroscopic) complex refractive index $n = 1 - \delta + i\beta$, where $i$ is the imaginary unit. The imaginary part $\beta$ of the complex refractive index is related to the linear attenuation coefficient $\mu = 4\pi\beta / \lambda$ where $\lambda$ is the x-ray wavelength. The linear attenuation coefficient gives the intensity loss caused by photoelectric absorption per unit path length traversed by the x-ray beam. The quantity $\delta$, i.e.
the deviation from unity of the real part of the refractive index, accounts for the phase shift experienced by the x-ray wave traversing the sample.

In absorption imaging the difference in linear attenuation coefficients of different materials provides image contrast. Phase imaging instead originates from the differences between materials in the real parts of the refractive index. In addition, single or multiple refraction shifts produced by features whose size is below the resolution limit are not directly resolved but rather contribute to an apparent decoherence (i.e. reduction of contrast) in the phase contrast image [20–26]. Such “unresolved” refraction effects are accounted for via ultra-small angle scattering.

Analyzer-based imaging, grating interferometry and coded apertures are sensitive to the variance \( \sigma^2 \) of the angular scattering distribution [10, 25, 26]. This variance is obtained by measuring the decrease of the contrast of the transmission function of the optical system (analyzer crystal, gratings or apertures) when the sample is in the beam. It was shown that the variance grows linearly with the traversed sample thickness \( z \) [20–23]. In fact, in Bech et al. [23], a thickness-independent linear diffusion coefficient \( \varepsilon = \sigma^2 / z \) was introduced quantifying the rate at which photons are removed from the primary beam by scattering. Its role is completely analogous to the role of \( \mu \) for absorption. Unlike the methods above, REI does not directly measure the variance. Rather, it directly measures the intensity \( I \) in a region of “dark” pixels which is proportional to the number of scattered photons. Nevertheless we expect this quantity to be proportional (via the imaging geometry and the detector efficiency), to the total thickness of the scattering sample. Therefore we expect a scattering measurement performed using REI to be compatible with different approaches based on the other techniques mentioned above.

3. Experimental results

To confirm this quantitative prediction, we used a sample made of optical paper, displaying negligible absorption and phase shifts. Data were taken at the x-ray laboratory located at the School of Physics, Monash University, Australia. The x-ray source was a rotating anode (Rigaku FrE + Superbright) with Cu target and accelerating voltage set to 45 kV. A pair of parabolic multilayer mirrors (AXO Dresden) was placed downstream of the source to collimate the beam and also provide effective monochromatization at a wavelength \( \lambda = 0.15 \) nm. Two sets of slits, located after the mirror pair, were used to define the beam size and to further reduce the divergence. The measured divergence was \( 0.18 \pm 0.01 \) mrad with a beam size of about 350 \( \mu \)m (FWHM) at the detector position. Data were acquired using the Medipix2 detector, featuring 55 \( \mu \)m pixel size. A detailed discussion of the sensitivity of the experimental setup can be found in [18]. The measurement of the scattered intensity was made in a single pixel row, directly behind the mirror shadow, even though, as depicted in Fig. 1, the scattering usually spans several pixels. The reason is that measuring in the region

Fig. 2. (a) Dark field x-ray image of a stack of optical paper tissues with variable thickness. The leftmost region corresponds to one paper sheet while the rightmost region corresponds to scattering from a stack of 6 optical paper sheets. Image data have been background subtracted, the said background corresponding to the intensity image measured in the absence of the paper. (b) Plot of the average counts in regions of equal thickness against the paper stack thickness (filled diamonds). The red solid line gives the linear fit to the data.
obscured by the mirror guarantees a much lower background, especially avoiding the scattering of the direct beam from the downstream slits and (in part) from the mirror surface.

Fig. 3. Multi-modal x-ray imaging of the abdomen of a house fly. (a) Attenuation image, (b) Refraction angle image, (c) Phase image, (d) Scatter (dark-field) image and (e) Absorption-free image (see text for details). The linear structures on both sides of the sample are the edges of a kapton foil, rolled to form a conical shape, used to hold the sample in place during the scan.

The first sample was constructed by stacking an increasing number of optical paper sheets, each with measured thickness of $20 \pm 1 \mu m$. Each subsequent sheet was transversely displaced with respect to the previous one thereby producing a homogeneous scattering object with variable thickness. The measurement of the paper sample scanned across the beam is in Fig. 2(a) showing the dark field image (number of counts in an otherwise dark row of pixels) for different positions of the sample. The exposure time was 5 s per step. The leftmost section corresponds to one paper sheet and the rightmost contains six superimposed paper sheets.

In Fig. 2(b) the average number of counts, calculated within regions of constant sample thickness and subtracted by the background noise (i.e. the intensity measured without the sample), is plotted against the sample thickness (filled diamonds). The red line corresponds to
the linear fit yielding a value $0.008 \pm 0.001 \, \mu m^{-1}$ for the slope and $0.01 \pm 0.09$ for the intercept. The latter value is compatible with 0, which is the nominal value of the intercept, corresponding to the scattering counts in the absence of the sample. Therefore the experimental data are in excellent agreement with the expected linear behavior of the scattered intensity with the sample thickness. Thus the data are in agreement with the claim that the scattered intensity, as measured by the REI setup, is proportional to quantitative dark-field measurements taken with other techniques [20–23], when the sample absorption is negligible.

An example of multi-modal imaging of a biological sample is shown in Fig. 3. The abdomen and part of the leg of a house fly (Musca domestica) are imaged. The exposure time in this case was 10 s per step. Attenuation, refraction and phase images were obtained using the method described in [18]. They are shown in panels (a), (b) and (c) respectively. The phase image was obtained by integration of the refraction (i.e. the differential phase) image. To reduce the noise arising from the numerical integration, a procedure based on the Fourier derivative theorem implemented via the fast Fourier transform, was applied. Details about the numerical post-processing procedure of the phase image can be found in [18]. The scatter image obtained during the same scan is shown in Fig. 3(d). Interestingly, it highlights features that are not visible in the other imaging modalities. On the other hand it shows poor contrast in the thickest part of the fly abdomen, which produces strong absorption and phase contrast.

The relative contribution of absorption and scattering to the images measured by REI deserve further analysis. The attenuation image displayed in Fig. 3(a) contains the contribution of both photoelectric absorption and scattering. Similarly, the scattered intensity (Fig. 3(d)) also depends on the sample absorption, and the two contributions are not decoupled. We can model the two images, considering the effect of both absorption and scattering as follows:

\[ A = e^{-\mu t} e^{-\varepsilon t}, \quad (1a) \]
\[ S = a \left(1 - e^{-\varepsilon t}\right) e^{-\mu t}. \quad (1b) \]

In Eq. (1a), $A$ represents the attenuation image assumed to be background subtracted and flat-field corrected, $\mu t$ is the projection of the object’s linear attenuation coefficient along the optic axis, and $\varepsilon t$ is the projection of the linear diffusion coefficient along the same axis; for all of these quantities, dependence on transverse coordinates is suppressed. Both absorption and scattering contribute to remove photons from the primary beam. The scatter image $S$ is modeled in Eq. (1b). Such an equation assumes that the scattered intensity, $1 - e^{-\varepsilon t}$, is itself attenuated by the sample absorption and collected with efficiency $a < 1$ (which depends on the geometry of the experiment). The simple model presented here is valid as long as the sample can be considered thin and the scattering to be restricted to very small angles.

The simple model previously introduced makes it clear that, unlike methods such as analyzer-based imaging, grating interferometry or coded apertures, REI cannot retrieve pure absorption and scattering images in a single scan, unless the parameter $a$ is known. On the other hand one can always calculate an absorption-free image by considering the ratio $S / A = a \left(1 - e^{-\varepsilon t}\right) / e^{-\varepsilon t} = a \left(e^{-\varepsilon t} - 1\right)$. Such an additional image is obviously not proportional to a pure dark-field image, but it does not contain absorption contributions. It can be interpreted as proportional to the scatter image amplified by the scattering attenuation. This absorption-free image is displayed in Fig. 3(e), which outlines different features of the sample which are difficult to distinguish in the scatter image alone.

A final remark concerns the stability of the optical setup used here. The measurements shown in Figs. 2 and 3 were acquired at different times spanning three days without the need to re-align the mirror. Therefore the stability of the mirrors (and the optical system as a whole) is extremely good, at least for the resolution attained in the present report.
4. Conclusions

In conclusion we have shown that the technique of x-ray reflective edge illumination (REI) is capable of multi-modal imaging of a specimen, obtaining with the same scan quantitative absorption, refraction and scattering contrast. A paper sample, featuring negligible absorption and phase contrast, was used to demonstrate that the scattering signal varies in accord with the sample thickness. Subsequently a house-fly specimen was imaged as a proof-of-concept biological application. Unlike other techniques, based on multiple acquisitions, REI cannot retrieve pure absorption and scatter images, unless the geometrical efficiency of the scattering collection is known. On the other hand the REI technique is extremely well suited to laboratory x-ray sources and therefore it can be potentially used in biological imaging.

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