This review provides a brief overview, albeit from a somewhat personal perspective, of the evolution and key features of various hard X-ray phase-contrast imaging (PCI) methods of current interest in connection with translation to a wide range of imaging applications. Although such methods have already found wide-ranging applications using synchrotron sources, application to dynamic studies in a laboratory/clinical context, for example for in vivo imaging, has been slow due to the current limitations in the brilliance of compact laboratory sources and the availability of suitable high-performance X-ray detectors. On the theoretical side, promising new PCI methods are evolving which can record both components of the phase gradient in a single exposure and which can accept a relatively large spectral bandpass. In order to help to identify the most promising paths forward, we make some suggestions as to how the various PCI methods might be compared for performance with a particular view to identifying those which are the most efficient, given the fact that source performance is currently a key limiting factor on the improved performance and applicability of PCI systems, especially in the context of dynamic sample studies. The rapid ongoing development of both suitable improved sources and detectors gives strong encouragement to the view that hard X-ray PCI methods are poised for improved performance and an even wider range of applications in the near future.
1. Introduction and overview

The observation of new physical phenomena and their understanding on the basis of accepted physical laws are the essence of progress in science. However, there can be significant time delays between the first and second ingredients being realized even though the underlying physics required may be well known. This review seeks to give a brief overview of the evolution of X-ray phase-contrast imaging (PCI) in various forms and to reflect en passant upon some of the phases in the development of the field, albeit from a somewhat personal perspective. In this process, it seeks to trace some of the key ideas and works involved in the evolution of X-ray PCI with a view to looking at the comparative advantages and limitations of the main hard X-ray PCI techniques currently in practice, particularly in the context of applications using conventional laboratory sources [1]. There have been a number of valuable recent reviews of hard X-ray PCI, in general [2], and some especially in the context of using synchrotron sources, for example [3]. This review tries to focus on methods that are of current interest in connection with hard X-ray applications using compact laboratory sources and the relevant issues with regard to performance.

A key quantity involved in the interaction of electromagnetic radiation with matter is the complex refractive index, namely

\[ n(r, E) = 1 - \delta(r, E) - i\beta(r, E), \]  

(1.1)

here expressed in the usual form for X-rays, where \( \delta, \beta \ll 1 \). The expressions for \( \delta \) and \( \beta \) away from an absorption edge may be found in [4]. For present purposes, we note that in the regime dominated by photoelectric absorption

\[ \delta(r, E) = \frac{r_0 h^2 c^2}{2\pi E^2} \rho(r) \sim O\left(\frac{1}{E^2}\right), \]  

(1.2a)

whereas

\[ \beta(r, E) = \frac{hc}{4\pi E} \mu_o(r, E) \sim O\left(\frac{1}{E^4}\right), \]  

(1.2b)

where \( E \) is the photon energy, \( \rho \) is the electron density, \( \mu_o \) is the photoelectric component of the linear attenuation coefficient, \( r_0 \) is the classical electron radius. As is well known, the \( \beta \) term leads to normal absorption while the \( \delta \) term leads to purely refractive contributions.

In considering imaging with electromagnetic radiation, we term images that contain features arising from the purely refractive term, \( \delta \), in the complex refractive index above (and are related to interference effects that are recorded via intensity distributions), phase-contrast images.

In this review, we first trace some early observations of PCI in the visible light context as a lead in to considering some of the manifestations in which X-ray PCI has been developed in recent times.

For a wave initially propagating along the optic axis assumed in the \( z \)-direction and undergoing a phase change \( \phi(r_{\perp}) \) in the \( r_{\perp} = (x, y) \)-plane (at right angles to \( z \)-direction) on passing through a thin object (such that the projection approximation is valid), this phase change is given by

\[ \phi(r_{\perp}; z, k) = -k \int_{-\infty}^{z} \delta(r_{\perp}, z'; k) dz' = -\frac{2\pi r_0}{k} \int_{-\infty}^{z} \rho(r_{\perp}, z') dz' = O\left(\frac{1}{E}\right), \]  

(1.3)

where \( k = 2\pi/\lambda = 2\pi E/hc \), so that the \( x \)-component of angle of deviation from the propagation direction, \( \Delta\alpha_x \), for small phase gradients owing to \( \delta \) is given for X-rays by [1]

\[ \Delta\alpha_x \approx -\frac{1}{k} \frac{\partial \phi(x, y; k)}{\partial x} \approx O\left(\frac{1}{E^2}\right), \]  

(1.4)

while we might note by comparison that the scattering angle in SAXS/USAXS in the kinematical approximation varies as \( 1/E \).
2. Historical background

(a) Optical imaging

(i) ‘Magic mirrors’ (ancient China and Japan)

Perhaps the earliest example of PCI being put into practice involves the art and demonstration of so-called ‘magic mirrors’ [5–7] that date back to at least the fifth century CE in China and apparently even earlier to the Han Dynasty (206 BCE–24 CE) [7,8], and, the performance of which remained steeped in mystery until the twentieth century. The basic feature of these magic mirrors lay in the fact that a cast or embossed design on the back surface of these bronze mirrors became visible when the highly polished and smooth convex front surface of the mirror was illuminated by direct sunlight and the reflected beam from the front surface of the mirror projected on to a wall. This magnified image of the back surface of the mirror did not involve any apparent focusing effect and was equally sharp at almost any distance. It appeared to have the mystical quality of imaging the back surface of the mirror by visible light penetrating the thick bronze mirror (typically of order, say, 5 mm thick) with no apparent features existing on the polished reflecting surface. Such mirrors were also known in Japan and termed ‘Makyoh’ for ‘wonder mirror’.

Although the properties of magic mirrors were known in the West from 1832, a proper explanation for their imaging properties baffled scientists for around 100 years until 1933 when W. H. Bragg [5,6,9] provided a satisfactory explanation, in general, physical terms for their properties. The underlying explanation was due to height distortions in the front surface of the mirror, believed caused by strains induced when polishing the front surface of the mirror as a result of the structure on the back surface. These minute height distortions led to visible light images of the back-surface structure being produced in the reflected beam via Fresnel diffraction in the near-field regime [6].

According to the analysis provided by Berry [6], the relationship between image intensity and height deviations from an assumed ideal spherical form for the convex mirror is of Laplacian form, namely

\[ I(r_\perp, z) = 1 + z \nabla^2 h(r_\perp), \]  

(2.1)

where \( h(r) \) is the height deviation (surface relief) of the mirror and \( r_\perp = (x, y) \) denotes position in the mirror reference plane and \( z \) is a reduced distance that asymptotes to \( R_0 \), the mirror radius, as distance from source to mirror and mirror to observation plane become large. The form of equation (2.1) clearly indicates that the form of the image is invariant with respect to change in the reduced distance, and the treatment lies within a geometrical optics approximation.

A key feature predicted by Berry’s treatment is the presence of black–white fringes at the edges of sharp height distortions. Such fringes are observed to be bright–dark when the step on the mirror surface goes from low to high and vice versa for high to low steps.

(ii) Contrast by defocus in early optical microscopes (Antoni van Leeuwenhoek)

Although not the inventor of the optical microscope, in his pioneering experiments with his early optical microscopes (1670s), van Leeuwenhoek was able to observe bacteria for the first time in 1683. His microscopes were quite simple and involved a single tiny spherical lens, essentially a magnifying glass, but of such small focal length that he could achieve magnifications of up to approximately 300 times [10].

His method of lens-making involved manufacture of miniature glass spheres by fusing of glass and was a key and well-kept secret that gave him a competitive advantage. He carried out numerous microscopic studies of biological organisms and other samples that were recorded in hand-drawn sketches, and in 1673 (at the age of 40) published his first paper (in Philosophical Transactions of the Royal Society, vol. 8, pp. 6037–6038, 6116–6118).

In his microscopic studies of bacteria, it is inevitable that structures he studied would have become more readily visible if they were observed slightly out of focus. This very early work
was followed around 250 years later by Zernike’s [11] development in 1932 (patented 1934) of the optical phase-contrast microscope, involving a phase plate introduced in the back-focal plane to help convert phase shifts produced by the sample into intensity variations in the imaging plane, that opened up imaging of unstained biological cells.

(b) Developments in X-ray phase-contrast imaging

(i) X-ray interferometry using single crystals (IB-PCI)

The earliest example of X-ray PCI lies in the work of Bonse & Hart [12,13] published in 1965. Using a Laue-Laue-Laue monolithic X-ray interferometer and a laboratory tube source in line-focus mode, they recorded thickness fringes in an X-ray interferometer for a thin plastic plano-concave epoxy plate that essentially acted as a pure phase object [13]. Subsequent, early work by Ando & Hosoya [14] further helped to demonstrate the potential of this technique. In this case, the image recorded phase changes induced in the wavefront by the sample, albeit modulo $2\pi$. For simple objects, the phase unwrapping problem can readily be handled to yield the phase change induced by the sample.

Impressive applications of this technique to biological samples demonstrating very high sensitivity to minute electron density differences in biological samples have been achieved by Momose and co-workers [15,16].

(ii) Double-crystal (or analyser)-based methods (AB-PCI)

Here, the first crystal acts as a monochromator/collimator, whereas the second crystal acts as an angular or spatial frequency filter. The wider the rocking curve of the analyser crystal, the greater the angular acceptance (spatial frequency bandpass) of the information recorded in the image. Wavefront distortions produced by the sample are modulated and filtered by dynamical scattering in the analyser crystal and free-space propagation. In most cases, the detector is close to the sample, and propagation effects after the sample are typically ignored.

This approach has a long history with various groups having made significant contributions. The earliest would appear to be those of Goetz et al. in 1979 [17] and Forster et al. in 1980 [18], both works involved the use of a double-crystal diffractometer to image a weakly absorbing sample, namely a fusion pellet. Impressive application of the double-crystal technique to biological samples was demonstrated by Ingal & Beliaevskaya [19]. Davis et al. [1] used a monolithic double-crystal arrangement to demonstrate key properties of the AB-PCI approach, for example contrast reversal with change in sign of the rocking angle for a phase object. Ingal & Beliaevskaya [19,20] described methods for combining images, whereas Chapman et al. [21] developed methods for separating absorption and refraction information from AB-PCI images. This line of approach was termed diffraction-enhanced imaging (DEI) [21]. Regimes of AB-PCI have been discussed by Gureyev & Wilkins [22].

By the nature of the method, each AB-based image is sensitive only to the phase-gradient component lying in the plane of the diffraction apart from propagation-based effects. Determination of the other phase-gradient component requires a separate measurement or the invocation of appropriate boundary conditions (but this is often numerically unstable and tends to lead to artefacts), see [23]. An approach for recording two phase-contrast images (but with the same diffraction plane) simultaneously using a Laue-case analyser and extracting phase information has been described by Kitchen et al. [24,25].

Although the AB-PCI method was first developed using conventional laboratory sources, AB-PCI techniques have been widely implemented at synchrotron sources, because such sources readily provide high-intensity beams that are both quasi-monochromatic and quasi-planewave in character, and so are well matched to the acceptance properties of the monochromator. If conventional laboratory sources are used, the high degree of curvature of the wavefront is not well matched to the use of flat crystals. Some improvement in angular acceptance of the system...
can be achieved by the use of an asymmetric collimator–monochromator or potentially by the use of curved crystals.

Analysers-based imaging can yield very sensitive images, for example of soft tissue [26] and with low background owing to high angular selectivity of scattering from the sample. However, such analyser-based imaging suffers from the following disadvantages and limitations in terms of widespread application:

— need for high mechanical stability of the crystals;
— significant loss of intensity owing to filtering of energy spectrum by the monochromator. This will become worse at higher $E$. This poses a significant limitation on the use of conventional X-ray sources for AB-PCI;
— limited field of view (FoV) which is determined by the maximum practical size of crystals and Bragg diffraction condition;
— spatial frequency bandpass is proportional to the rocking curve width of the analyser crystal [27] and decreases as $E$ becomes large; and
— for moderate $E$, signal-to-noise ratio (SNR) and figure of merit (FoM) decrease only as $1/E$ [28,29]. As $E$ becomes large, the resolution of the system might be thought to degrade owing to increase in extinction, however this effect would appear to be compensated for owing to the change in projection on the image plane (see equation (4) in [23]; figure 1).

Application of AB-PCI methods for clinical medical diagnostics will need to overcome the various limitations indicated above. Some examples of significant progress in this area in the case of application to mammography can be found in [26].

(c) Pursuit of methods of phase-contrast imaging that do not require monochromatic X-rays

In our own work, after exploring aspects of AB-PCI [1,30] and conscious of the limitations of exploitation of AB-PCI with conventional sources, we sought other methods of PCI that did not necessitate using essentially monochromatic X-rays. Among them was an aperture-based method [31] that involved measuring the deflection of X-ray beamlets on introduction of a sample into the beam. Measurement of the distributions of beamlets (figure 2) recorded using a high spatial resolution detector offers the possibility of simultaneously measuring refractive, absorptive and scattering (SAXS) contributions made by the sample with essentially no strict requirement on monochromaticity or involving a loss of photons after passing through the sample. Such an imaging system has a requirement for highly collimated beamlets that might be produced using a microfocus source. The approach could readily be incorporated in a conventional radiographic-type imaging system with the possibility of rapid switching from conventional to aperture-based imaging mode. Requirements on energy bandpass are not very strict. We note that the refraction angle for the purely refractive contribution of the sample varies as $1/E^2$ (see equation (1.4)) which would affect the peak profile but one might expect not to affect the peak displacement to first-order (see also refs [31–33]). Deconvolution of the beamlet profiles for the known energy distribution of the beamlets may be beneficial if the source is not essentially monochromatic.

Various groups have developed and demonstrated aperture-based methods of X-ray PCI, including some involving only a single exposure of the sample, and that show promise for practical application in biomedical studies. These are discussed in more detail in the relevant section below.

(d) Propagation-based hard X-ray phase-contrast imaging (PB-PCI)

In the case of looking for early encounters with phase effects in (moderately hard) X-ray imaging, one might go back to the work of Cosslett & Nixon [34] on the projection X-ray microscope. Using a magnetically focused electron beam incident on a thin foil target as a microfocus X-ray
Figure 1. (a) Diagram showing one variant of analyser-based imaging also showing (b) monolithic monochromator-analyser system used, see [1]. (c) Comparison of a conventional-type radiograph and (d) an AB-PCI radiograph of a eucalyptus leaf recorded using the system with fixed analyser crystal shown in figure 1 [1]. Note that (d) is, in fact, a dark-field radiograph owing to tilt of analyser away from the exact Bragg condition, because vein structure is bright on a dark background.

Figure 2. Schematic outline of an aperture-based method of phase-contrast imaging, showing possible types of information that could be measured (adapted from [31]).
source, they observed Fresnel diffraction effects from samples, but were operating in the context of shadow microscopy and such effects were basically regarded as a form of unwanted blurring in the image and essentially to be avoided.

In our case, the quest for methods of PCI that did not involve the need for highly monochromatic radiation led us to more carefully analyse some experiments that we had carried out on imaging thin wood samples (around 100 µm thick) using a low-power laboratory-based microfocus source (Kevex, with nominal 10 µm spot size from a Cu target). We observed that the images changed as a function of the distance, $R_2$, between the sample and detector (X-ray film). Some examples of such images are illustrated in figure 3.

Although Fresnel diffraction seemed a possible explanation, the fact that we had an essentially polychromatic source seemed at first to point away from this explanation. However, further experiments with a variety of samples and varying the source–sample and sample–detector distance combined with theoretical considerations confirmed the basic explanation in terms of Fresnel diffraction [35,36], especially when imaging weakly absorbing objects.

Key features of the Fresnel-diffraction-based approach to propagation-based PCI can be seen from the expression below for the intensity in the detection plane for diffraction from a pure phase object, namely

\[
I(Mx, My; R_1 + R_2; k) = \frac{I_0}{M^2} \left\{ 1 + \frac{R_2}{kM} \nabla^2 \phi(x, y; R_1, k) \right\}
\]

\[
= \frac{I_0}{M^2} \left\{ 1 - 2\pi \frac{r_o}{k^2} \frac{R_2}{M} \nabla^2 \int_{-\infty}^{R_1} \rho(x, y, z)dz \right\},
\]

(2.2)
Figure 4. Contrast transfer function for the contribution owing to \( \delta \) (purely refractive) in PB-PCI for perfect coherence (red curve) and for finite source size (blue curve). The green curve shows loss of features owing to finite source size. Based on [37].

where \( R_1 \) is the source-object distance and \( M = (R_1 + R_2)/R_1 \) is the geometrical magnification. Expression (2.2) can be derived from Fresnel diffraction in the paraxial approximation under a weak-object assumption (see [37]) or from the transport of intensity equation (TIE)

\[
-k \frac{\partial}{\partial z} I(r_\perp, z) = \nabla_\perp \cdot (I(r_\perp, z) \nabla_\perp \phi(r_\perp, z)) \\
\equiv \nabla_\perp I(r_\perp, z) \cdot \nabla_\perp \phi(r_\perp) + I(r_\perp, z) \nabla^2_\perp \phi(r_\perp, z),
\]

(2.3)

see, for example, references [2,38].

From expression (2.2), one can readily see that

— essentially pure phase objects will show no contrast in contact radiography mode but can show significant phase contrast, especially at sharp boundaries, in projection mode; and
— image structure in the near-field regime relevant to (2.2) is essentially independent of energy bandpass of the incident beam. This helpful and somewhat surprising finding makes PCI readily achievable, e.g. even with polychromatic laboratory microfocus sources (say \( \Delta E/E \leq 30\% \)), in a certain regime [37].

Importantly, the magnitude of phase-contrast is strongly determined by the lateral spatial coherence length of the incident wave in the object plane, namely

\[
l_{x,y} = \frac{\lambda R_1}{2.355\sigma_{x,y}(\text{src})}.
\]

(2.4)

For significant phase contrast to occur, \( l_{x,y} \) needs to be comparable to or larger than the inverse spatial frequency \( (1/u_{\text{feature}}) \) of the feature size of interest, see [37] and also figure 4 (CTF).

Related work for propagation-based imaging was published independently in the context of the synchrotron case by Snigirev et al. [39], using monochromatic radiation and a highly collimated parallel beam.
(e) Some key features of PB-PCI

The resolution for a propagation-based PCI system at the object plane is given by [40,41]

\[
\sigma_{\text{sys}}^2 \approx (1 - 1/M^2) \sigma_{\text{src}}^2 + M^{-2} \sigma_{\text{det}}^2 + \sigma_{\text{min}}^2, \tag{2.5}
\]

where \(\sigma_{\text{sys}}^2\) is the variance of the system point-spread function (assumed Gaussian) and \(\sigma_{\text{src}}^2\) and \(\sigma_{\text{det}}^2\) are the variances of the source distribution and the detector spatial resolution, respectively. The diffraction term, with \(\sigma_{\text{min}} = 1/(2(\lambda R^2/M)^{1/2})\), becomes significant beyond the first Fresnel zone but less significant for a given geometry as \(E\) becomes larger (cf. AB-PCI).

For a pure phase object, the contrast transfer function is illustrated in figure 4 and shows the loss of phase-contrast information both for large and small \(\xi = u\sqrt{\lambda z}\). For small \(\xi\), it is due to the intrinsic nature of propagation-based phase contrast and for large \(\xi\) it is due to geometrical blurring. The quantity \(1/u\) is the feature size of interest and \(\xi < 2^{-1/2}\) corresponds to the near-field regime. Equation (2.5) also forms the basis for geometrical resolution in other methods discussed below (see [28]).

(f) Wavefront sensing and coded aperture methods

Wavefront sensing in visible light optics may be traced back to the work of Hartmann at the turn of the twentieth century using regularly spaced apertures in an opaque material and improved upon by Shack using lenslet arrays and an imaging detector [42].

Various groups have recently developed and demonstrated coded aperture-based methods for hard X-ray PCI that show considerable promise for practical application in biomedical studies and potentially in clinical medical studies if suitable laboratory-based sources become available. In particular, the work of the following groups should be mentioned in this connection:

1. Olivo and co-workers [43–45] using two matched coded apertures one just before the sample and one just in front of the detector (or a high spatial resolution detector with sharp pixel boundaries). For each component of the phase gradient, two images are required.

2. Morgan et al. [46–48], who have used a single two-dimensional coded aperture in front of the sample combined with a high spatial resolution detector and correlation analysis of shifts in intensity in small regions of images taken with and without the sample in the beam, in order to simultaneously determine two components of the phase gradient. See also Wen et al. [49] for treatments of this general approach.

3. Krejci et al. [32,33,42,50], who have used subpixel resolution analysis with a micrometre-scale source and a high spatial resolution detector to determine very small displacements in two-dimensions of essentially rectangular profile X-ray beamlets to obtain both components of the phase gradient simultaneously from a single image. This has included studies at 70 kVp [32] (figure 5).

4. Mayo & Sexton [51] have used lenslet arrays to carry out Shack–Hartman-type wavefront analysis for less than 10 keV X-rays and this would also appear to be of interest for hard X-rays if suitable lenslet arrays can be produced.

All the coded aperture methods mentioned above have the potential to operate with fairly broadband radiation, which can be a considerable advantage for application with conventional sources. Methods (2) and (3), that involve only a single-coded aperture, appear to have stricter requirements on source size than method (1). In a general sense, single-coded aperture methods might be viewed as an extension of PB-PCI in that the combination of sample and coded aperture placed immediately in front of or behind the object may be effectively regarded as a single object.

However, one should note that for highly absorbing coded apertures, the further assumption often made that the intensity at the exit from the combined aperture-object is slowly varying is likely not to be valid. This means that simple theoretical treatments of wave propagation and
3. Grating-interferometer-based phase-contrast imaging

Grating-interferometer-based (GIB) methods of imaging contain elements of single-crystal interferometry, AB-PCI and PB-PCI. Early discussion of possible implementation of GIB methods for X-rays can be found in the work of Clauser [53,54], whereas practical implementation may be traced to the work of David et al. [55], who used a two-grating system plus analyser crystal (to filter out unwanted diffraction orders) and also to Momose et al. [56], who initiated implementation of a Talbot-grating-based (TGB) interferometer with two gratings alone and also demonstrated measurement of the phase gradient for a simple object. A detailed review of developments in TGB methods for X-rays can be found in a recent article by Pfeiffer [57].

A detailed consideration of the theoretical performance of grating-based imaging systems is given in [29,58]. There are significant requirements on spatial coherence relative to the first grating and lesser requirements on beam monochromaticity. Introduction of a linear aperture array in close proximity to the source (Talbot–Lau case) can increase the intensity in the image in proportion to the number of apertures but is at the expense of spatial resolution, because spatial resolution is determined by the width of the array, not the individual effective size of the sourcelets. Spatial resolution is also determined by the period of the gratings and/or detector resolution.

In principle, if a high spatial resolution detector (better than the Talbot fringe spacing) is available, only one grating, namely the phase grating, is required. This approach to grating-interferometer-based phase-contrast imaging (GIB-PCI) has been demonstrated by Takeda et al. [59].

Extension of the Talbot-grating-interferometer approach to the simultaneous determination of the two components of phase gradient using two-dimensional gratings has been described by Itoh and colleagues [60,61] and by Wu et al. [52].

4. Summary of key features of the five methods of phase-contrast imaging

In table 1, we try to summarize some of the key system performance requirements and limitations for the five different classes of PCI methods considered here. In preparing this, we have
**Table 1.** Comparison of basic system requirements for different hard X-ray phase-contrast imaging methods.

<table>
<thead>
<tr>
<th>phase-contrast imaging technique</th>
<th>optics</th>
<th>chromatic coherence requirements and performance at high E</th>
<th>spatial coherence of source requirements and limits on resolution</th>
<th>quantity sensed</th>
<th>comments and key issues for application with conventional sources, also some key references</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. interferometry using single crystals (IB-PCI)</td>
<td>monolithic single crystal</td>
<td>first-crystal wafer acts as a monochromator/beam splitter. Involves single-crystal-type bandpass</td>
<td>resolution is limited by source size/beam collimation and extinction length.</td>
<td>$\phi$</td>
<td>‘phase unwrapping’ problem needs to be treated as measured phase is modulo $2\pi$ single-crystal splitter/monochromator has low photon throughput and FoV limited by projected size of crystal in the plane of diffraction [12–15]</td>
</tr>
<tr>
<td>2. analyser-based (AB-PCI/DEI)</td>
<td>single-crystal monochromator and analyser</td>
<td>first crystal acts as a monochromator/collimator. Involves single-crystal-type bandpass</td>
<td>resolution is limited by same factors as PB-PCI and also in plane of diffraction by extinction length in analyser crystal, see [27–29]</td>
<td>$\nabla_x \phi$</td>
<td>only the component of the phase gradient in the plane of diffraction is directly derived from a single measurement (here denoted ‘x’), not well matched to a ‘point source’ $\Rightarrow$ small FoV (in plane of diffraction) and image distortion in out-of-diffraction-plane direction requires various additional assumptions on form of rocking curve and nature of wavefront for phase retrieval [1,19–21,27,30]</td>
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<tr>
<td>3. propagation-based (PB-PCI)</td>
<td>no optics needed</td>
<td>essentially, no bandpass restriction in near-field regime</td>
<td>high spatial coherence required. Resolution limited by source size ($M \gg 1$) and detector resolution ($M \approx 1$). Also by diffraction, unless in the near-field. See [40]</td>
<td>$\nabla^2 \phi$</td>
<td>can yield two-dimensional phase map directly from measured image or images. Essentially energy bandpass independent in near-field regime. No need for optics (therefore, low on aberrations). Can provide large FoV sensitive to sharp/small features but not very sensitive to broad features [29] resolution limited by source size or detector resolution and by diffraction at very high spatial resolution [31,35,37,39–41,62]</td>
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<tr>
<td>4 Shack–Hartmann/coded aperture methods in non-interferometric mode</td>
<td>two matched coded apertures</td>
<td>can operate with broad bandpass</td>
<td>resolution limited by size and spacing of apertures in the CA array</td>
<td>$\nabla_x \phi$</td>
<td>require high spatial resolution detector spatial resolution is ultimately limited by detector resolution (or source size), i.e. expression (2.5)</td>
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<tr>
<td>(i) coded aperture methods involving e.g. two two-dimensional gratings</td>
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<td>(ii) single absorber grating just prior to the object and use of single image of object</td>
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<td>(iii) subpixel resolution (Krejci and colleagues)</td>
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<td>(iv) using lenslet arrays</td>
<td>lenslet array</td>
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<tr>
<td>5. grating-based Interferometry (GIB-PCI)</td>
<td>phase grating adjacent to object and possibly one or more other gratings depending on source size and detector resolution</td>
<td>basic method is not very sensitive to $\Delta E/E$ but will involve dispersion and loss of performance owing to dispersion by sample</td>
<td>requires a high degree of spatial coherence. For broad source, can be obtained by use of source-grating, but this reduces spatial resolution. Spatial resolution limited by same expression as for PB-PCI and/or second grating period</td>
<td>$\nabla x \phi$</td>
<td>usually treated in geometrical optics approximation. System itself is not very sensitive to $\Delta E/E$, except for dispersion effects induced by the sample. Also bright- and dark-field modes of imaging possible given multiple images for stepped 2nd grating. See [56,65,66] Resolution effectively limited by expression (2.5), where source size is total source size in the Talbot–Lau case.</td>
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<tr>
<td>use of one or more gratings plus high spatial resolution detector to resolve Talbot images</td>
<td></td>
<td></td>
<td></td>
<td>$\nabla x \phi$</td>
<td>single grating methods, see Takeda et al. [59]. This area overlaps with single optic CA methods [32,46,48,50]</td>
</tr>
<tr>
<td>extension to two-dimensional gratings</td>
<td></td>
<td></td>
<td></td>
<td>$\nabla x, y \phi$</td>
<td>requires high spatial resolution detector [60,61]</td>
</tr>
</tbody>
</table>

*Table 1.* Continued.
particularly drawn on references [28,29,58], in addition to specific references mentioned elsewhere in this review.

Some general considerations relating to the performance of the various PCI methods are as follows:

— while some methods may be a form of incoherent imaging, a key parameter is angular source size viewed from the sample. When comparing different systems operating at the same energy, this quantity corresponds to a measure of lateral spatial coherence length;
— determination of a single component of the phase gradient does not unambiguously lead to phase retrieval in principle, unless the object is isolated in the direction perpendicular to the phase-gradient component measured. Even then, retrieval of the phase distribution, $\phi$, may be impractical due to artefacts introduced in the data analysis via noise;
— if broadband polychromatic radiation is used, then dispersion by the sample may affect the ability to determine the phase gradient;
— single-image methods are highly desirable, if the sample is not stationary in time or if the source of illumination is not stationary;
— avoidance of apertures after the sample, where possible, is desirable in order to minimize dose and maximize information gathered. New types of two-dimensional pixel-array detectors offer exciting possibilities for practical application of coded aperture methods that can provide subpixel resolution information with little crosstalk between pixels and even possibly energy analysis; and
— coded aperture methods can potentially simultaneously provide phase gradient, absorption and scattering (dark field) images from a single image.

5. Optimization of performance and comparative studies

A useful theoretical measure of the relative performance of different PCI methods at a given photon energy (or energy spectrum) is SNR for a given sample, feature and dose to the sample as well as given characteristics for source size and detector. A useful FoM in this regard is [28,29]

$$\text{FoM} = \frac{\text{SNR}}{D^{1/2}},$$

where the SNR is based on the number of photons detected, $D$ is the dose at the entry surface of the sample. This essentially quantifies the statistically significant information derived about a given feature per unit dose and allows useful comparison of quality of the information provided by different X-ray imaging methods.

While contrast afforded by a method is important, it might be noted that contrast is only one indication of performance, e.g. observing one photon in an experiment constitutes huge contrast, but provides essentially no information.

A theoretical comparison of performance parameters for AB-PCI, PB-PCI and GIB-PCI methods for a range of instrumental parameters and model samples has recently been published by Diemoz et al. [28] and also together with some related experimental studies [29], providing expressions and some experimental results for FoMs for each of the above methods. Of particular interest are the results for the variation of the FoM of the various methods with photon energy, $E$, which were presented by these workers, namely, PB-PCI ($1/E^2$), AB-PCI ($1/E$) and GIB-PCI ($1/E^2$). These results all assume a certain fluence (photons/area), $I_0$, incident on the sample such that dose, $D = K_{\text{dose}}I_0$, where $K_{\text{dose}}$ depends on sample properties and $E$.

In considering the relative merits of different PCI methods for a particular application and feature type, as well as a particular X-ray source, the following cases might typically arise:

(1) the selected imaging method and desired SNR is dose limited, or
(2) it is exposure-time (i.e. X-ray source power) limited.
If case (1) applies, then expression (5.1) is a useful practical measure of performance of a method. However, if case (2) applies, then the relative efficiency of the different methods and their specific configurations in using a given source becomes relevant.

To help to give practical guidance in regard to the relative merits of different methods and configurations for case (2), i.e. when they are exposure-time limited, we here introduce an additional figure-of-merit-type quantity, namely the efficiency

\[
\text{Eff}(\text{method}; \text{source}) = \frac{\text{SNR}}{\text{time}^{1/2}} = \text{FoM} \times \text{dose rate}^{1/2},
\]

which may be viewed as the rate of information collection for a given PCI method and experimental implementation. For present purposes, a crude approach to describing the factors affecting the dose rate might be expressed by

\[
\text{dose rate}(\text{method}; \text{source}) \propto \frac{\Delta E}{E} \times B \times S_{\text{area used}} \times f \times \frac{1}{n},
\]

where \(B\) is the brightness of the source (photons mm\(^{-2}\) s\(^{-1}\) per 0.1\% bandpass), \(S_{\text{area used}}\) is the area of the source that contributes to the dose at the entry plane to the sample, \(\Delta E\) is the energy bandpass of the imaging system for the given source, \(f\) is the fraction of photons that are transmitted to the entry plane of the object (e.g. after losses owing to apertures and possible gains by focusing effects), whereas \(n\) is the number of images required to obtain the final image.

On this basis, we note, for example, that while AB-PCI would appear to have the best trend for an FoM given by equation (5.1) as \(E\) becomes large, \(\Delta E/E\) for AB-PCI will vary roughly as \(1/E\) owing to reduced energy bandpass of the monochromator for AB-PCI, but not vary much with \(E\) for the other methods considered here.

It should also be remarked that any comparison of relative performance of different methods inevitably involves the selection of a model sample, and so any comparison of methods would be, to a greater or lesser extent, sample-specific. For detailed comparison of specific methods, configurations, model samples and operating conditions, computer simulation can provide a very convenient, efficient and flexible approach, and is the one that we and others have used widely.

6. Phase retrieval and omnimicroscopy

The various methods of PCI mentioned above become unified when one includes quantitative phase retrieval as an outcome of the investigations. This has now become a major focus of activity in the X-ray imaging area and extends to phase-contrast computerized X-ray tomography. Basically, it involves inverting the diffraction problem to determine the exit wave function for the object and thereby both the absorption and projected electron density, via (1.3). In the case of propagation-based imaging for X-rays, the earliest demonstration lies in the work of Nugent et al. [67] and was based on solution of the TIE (see equation (2.3)). There are many variants of the approach to phase retrieval for PB-PCI including using images at two or more distances, e.g. holotomography (see Cloetens et al. [68]) and TIE-based [69], multi-energy phase retrieval [70] and the single-homogeneous material case [71] that is widely used.

For methods of PCI that measure only a single gradient of the phase, phase retrieval, while theoretically possible for objects isolated in at least one direction, can involve instabilities and artefacts as mentioned earlier. Given that methods are becoming available that can determine both gradients of the phase simultaneously at each point in the image, these would seem to be preferable.

Detailed discussion of phase retrieval methods lies outside the scope of this review. However, it is perhaps useful to note the unifying role that phase/amplitude determination plays with regard to the different PCI methods which is outlined in the article by Paganin et al. on ‘Omnimicroscopy’ [72], where the determination of the phase and amplitude modulation at the exit surface of the object by one method in principle allows the generation of synthetic images for any of the other PCI methods.
7. Conclusion

The field of hard X-ray PCI is rapidly developing on many fronts. This review has tried to give a brief overview of the development and key features of the main classes of methods, including some, which are at an emerging stage and which appear to have some desirable features. Among desirable features for widespread practical application in general are ability to be readily and be efficiently implemented on conventional sources, ability to record complete information in a single image/exposure, mechanical simplicity and stability as well as moderate cost.

Practical application of PCI to static objects using conventional sources is already well developed. However, a major limitation at the present time in studies of dynamic systems and especially in vivo studies is the low brilliance of conventional/laboratory sources compared with synchrotrons. Using synchrotron sources, PCI methods have found widespread application to in vivo biomedical and also some clinical medical areas, but transition to in vivo laboratory-/clinic-based applications has been slow. Notwithstanding, some promising areas for early application of laboratory-based PCI in the biomedical and medical context would appear to be where dose and/or exposure time is not important, e.g. biopsies and where a small FoV is of interest, e.g. region of interest diagnostics and where suitable high spatial resolution detectors may already be available. Application to a wider range of clinical and biomedical studies awaits the development of higher performance laboratory X-ray sources and large-area high-performance detectors suited to the implementation of hard X-ray PCI methods mentioned here. These are technologies that are undergoing rapid advances at the present time, which bodes well for widespread practical application of PCI methods in the near future.

In conclusion, we might recall the words of Fritz Zernike in the context of phase-contrast optical microscopy, namely that “I went in 1932 to the Zeiss Works in Jena to demonstrate. It was not received with such enthusiasm as I had expected. Worst of all was one of the oldest scientific associates, who said ‘If this had any practical value, we would ourselves have invented it long ago’ “ with the hope that this barrier is not encountered in applications of X-ray PCI methods.

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References


20. Ingal VN, Belyaevskaya EA, Efanov VP. 1995. High energy computerised axial tomography irradiating object by X-ray beam with wide wave front and determined divergence and setting crystal-analyser to obtain Bragg reflection conditions. Patent no. WO9221016-A; RU2012872-C.


