Robustness of phase retrieval methods in x-ray phase contrast imaging: A comparison

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Purpose: The robustness of the phase retrieval methods is of critical importance for limiting and reducing radiation doses involved in x-ray phase contrast imaging. This work is to compare the robustness of two phase retrieval methods by analyzing the phase maps retrieved from the experimental images of a phantom.

Methods: Two phase retrieval methods were compared. One method is based on the transport of intensity equation (TIE) for phase contrast projections, and the TIE-based method is the most commonly used method for phase retrieval in the literature. The other is the recently developed attenuation-partition based (AP-based) phase retrieval method. The authors applied these two methods to experimental projection images of an air-bubble wrap phantom for retrieving the phase map of the bubble wrap. The retrieved phase maps obtained by using the two methods are compared.

Results: In the wrap's phase map retrieved by using the TIE-based method, no bubble is recognizable, hence, this method failed completely for phase retrieval from these bubble wrap images. Even with the help of the Tikhonov regularization, the bubbles are still hardly visible and buried in the cluttered background in the retrieved phase map. The retrieved phase values with this method are grossly erroneous. In contrast, in the wrap's phase map retrieved by using the AP-based method, the bubbles are clearly recovered. The retrieved phase values with the AP-based method are reasonably close to the estimate based on the thickness-based measurement. The authors traced these stark performance differences of the two methods to their different techniques employed to deal with the singularity problem involved in the phase retrievals.

Conclusions: This comparison shows that the conventional TIE-based phase retrieval method, regardless if Tikhonov regularization is used or not, is unstable against the noise in the wrap's projection images, while the AP-based phase retrieval method is shown in these experiments to be superior to the TIE-based method for the robustness in performing the phase retrieval.

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Key words: x-ray imaging, phase contrast, phase retrieval

I. INTRODUCTION

In recent years, the in-line phase-contrast x-ray imaging has attracted intensive research efforts. The in-line phase-contrast x-ray imaging is a technique using the free space diffraction of phase-shifted x-rays to form the interference fringes at tissues' boundaries and interfaces in images.^{1–8} In fact, for over 100 years, the tissue attenuation differences have been the sole contrast mechanism for medical x-ray imaging. However, when x-rays traverse the body parts, as a wave x-rays undergo phase shifts as well. The amount of the phase shift along an exit ray is determined by the tissue refractive indices along the ray. Note that x-ray refractive index n is a complex number and equal to $n = 1 - \delta + i\beta$, where δ is the refractive index decrement and responsible for x-ray phase shift, while β is the imaginary part of the refractive index and responsible for x-ray attenuation. The amount of x-ray phase shift along an exit ray is given by $\varphi = -(2\pi/\lambda) \int \delta ds$, where λ is the x-ray wavelength, and

the integral is over the ray path.^{1,2} In other words, the phase shift is equal to the projection of refractive index decrements scaled by a factor $(2\pi/\lambda)$. On the other hand, x-ray attenuation along an exit ray is determined by the projection of the tissue linear attenuation coefficients along the ray, which is equal to $(4\pi/\lambda) \int \beta ds$.^{1,2} We have estimated δ and β values for the biological tissues and found that the tissue δ values (10^{-6} – 10^{-8}) are about 1000 times greater than their β values (10^{-9} – 10^{-11}) for 10–150 keV x-rays.⁸ Hence, the differences in x-ray phase shifts between different tissues are about 1000 times greater than their differences in the projected linear attenuation coefficients. Therefore, the phase-contrast imaging techniques may greatly increase the lesion-detection sensitivity for x-ray imaging. The settings for the inline phase-sensitive imaging are similar to that of conventional x-ray imaging, provided a source with very small focal spot and a sufficiently large object-detector distance are required.^{5,7,8} In the inline imaging setting, x-rays undergo phase shifts as traversing the imaged object, and then diffract

freely over a sufficiently large distance before reaching the detector. In this way, the tissues' phase contrast manifests as the dark-bright diffraction fringes at tissues' boundaries and interfaces in the measured images.^{5,7,8} Hence, the inline phase contrast imaging has good potential of greatly enhancing the detection sensitivity and reducing radiation doses involved in the imaging.

However, as the interfaces and boundaries of the different tissue compartments are greatly accentuated in a phase-contrast image, the bulk phase contrast in a given tissue compartment, where the phase shifts may vary slowly, could get lost. This is because the phase contrast is proportional to the Laplacian and gradient differentials of the phase shifts, as is shown in Sec. II below. Moreover, the information about x-ray phase shifts are valuable for tissue characterizations, since x-ray phase shift along a ray is proportional to the projected tissue electron density, that is, $\varphi = -\lambda r_e \int \rho_e ds$, where r_e is the classic electron radius and ρ_e denotes the tissue electron density and the integral is over the ray path.^{1,2} In order to fully exhibit tissue phase contrast and reconstruct tissue projected electron densities for quantitative tissue characterizations, one needs to extract the tissue phase shifts from the mixed contrast exhibited in a phase-sensitive projection. The procedure of retrieving the phase-shift map of an object from its phase-sensitive projections is called the phase retrieval.^{10–14} A retrieved phase map is able to provide a quantitative map of the object's projected electron densities, which could be used for quantitative tissue characterizations.^{12–14} Moreover, performing phase retrieval is necessary for reconstructing volumetric 3-D maps of tissue attenuation coefficients and refractive indices, respectively,^{14,15} and for eliminating the phase-contrast caused artifacts in the volumetric 3-D images.¹⁶

Examining the robustness of phase retrieval methods against the projection noise, such as the x-ray photon quantum noise and others involved in the projection acquisitions, is an important task in phase contrast imaging. If a phase retrieval method is not robust against the noise, the method could become unstable and fail in phase retrievals if the acquired projection images had been contaminated with substantial noise. On the other hand, suppressing x-ray quantum noise may require using high radiation doses in the image acquisitions. For clinical applications, it is imperative to limit and reduce radiation doses involved, hence, it is critical to develop robust phase retrieval methods for future clinical applications of phase contrast imaging. The purpose of this work is to compare the robustness of two phase retrieval methods by means of analyzing the phase maps retrieved from the experimental projection images of an air-bubble wrap phantom. We will first introduce the phase retrieval method that is based on the transport of intensity equation (TIE), which describes how the phase contrast is encoded in the projection images.^{10,11} This TIE-based method is the most commonly used method for phase retrieval in the literature. We will then introduce a recently developed phase retrieval method, namely the attenuation-partition based (AP-based) method.¹³ In order to examine the robustness of these two methods against noises, we applied these two phase re-

trieval methods to experimental phantom images, namely a radiograph and a phase contrast image of the air-bubble wrap phantom, for the phase retrievals. We will analyze the retrieved phase maps obtained by using the two methods and compare their performances in the robustness against noises in the phantom images. In Sec. IV, we explain that these performance differences of the two phase retrieval methods are rooted in their different techniques employed to deal with the singularity problem involved in the phase retrievals. In addition, other factors that may affect the phase retrieval performance will be briefly discussed as well.

II. PHASE RETRIEVAL METHODS

In phase contrast images, the attenuation contrast and phase contrast are mixed together. In order to retrieve phase maps from phase contrast projection images, one should understand how the phase contrast is encoded in the projection images. This understanding can be gained from the x-ray propagation equation such as the TIE.^{10,11} This equation can be derived either from the x-ray Fresnel-diffraction equation or the Wigner distribution based phase-space formalism.^{9–11} If we denote the x-ray transmission image of an object, or equivalently its x-ray attenuation map by $A_o^2(\vec{r})$ and the x-ray phase-shift map of the object by $\varphi(\vec{r})$, then the detected x-ray intensities are given by^{8,11,17}

$$I(\vec{r}_D) = \frac{I_{in}}{M^2} \left\{ A_o^2(\vec{r}_D/M) - \frac{R_2 \bar{\lambda}}{2\pi M} \nabla \cdot (A_o^2(\vec{r}_D/M) \nabla \varphi(\vec{r}_D/M)) \right\} \quad (1)$$

where $\bar{\lambda}$ is the average x-ray wavelength of the polychromatic x-rays. In Eq. (1), I_{in} is the entrance x-ray intensity, R_1 is the source-object distance set in the projection, R_2 is the object-detector distance, $M = (R_1 + R_2)/R_1$, the magnification factor in the projection, and $\vec{r}_D$ denotes the position vector in the detector plane. In Eq. (1), the operator ∇ denotes the two-dimensional transverse gradient differential operator. For the purpose of this work, we assume that the x-ray source's focus spot is ideally point-like and the detector employed is an ideal detector. Obviously, the detected x-ray intensity $I(\vec{r}_D)$ is determined not only by attenuation map $A_o^2(\vec{r})$ in the projection, but also by the encoded phase contrast, that is, by the transverse Laplacian and gradient differentials of the phase-shift map $\varphi(\vec{r})$ in the projection. Since the phase contrast and attenuation contrast are mixed together in a phase contrast image, as is shown by Eq. (1), hence measuring a single phase-contrast image is not enough for retrieving the phase-shift map $\varphi(\vec{r})$ in the projection. Therefore, in general, at least two projection images are needed for retrieving the phase-shift map $\varphi(\vec{r})$ of the object.

The most commonly used phase retrieval method in the literature is the TIE-based method. In this method, two acquired projection images of an object are used for retrieving the phase-shift map of the object: one is a contact radiograph $A_o^2(\vec{r})$ of the object, the other is a phase contrast projection image $I(\vec{r}_D)$ of the object. One then is able to retrieve the phase-shift map $\varphi(\vec{r})$ by solving Eq. (1) for $\varphi(\vec{r})$ as follows¹²:

$$\varphi(\vec{r}) = - (2\pi M / \bar{\lambda} R_2) \nabla^{-2} \times \left\{ \nabla \cdot \left[\frac{1}{A_o^2} \nabla \left(\nabla^{-2} \left(\frac{M^2 I}{I_{in}} - A_o^2 \right) \right) \right] \right\}. \quad (2)$$

In above equation, the operator ∇^{-2} denotes the inverse of the Laplacian differential operator $\nabla^2 \equiv (\partial^2/\partial x^2 + \partial^2/\partial y^2)$. The inverse Laplacian operator ∇^{-2} is a pseudodifferential operator. The action on a function $g(\vec{r})$ of a pseudodifferential operator such as ∇^{-2} is defined as

$$\nabla^{-2} g(\vec{r}) \equiv \iint \exp(i2\pi(\vec{s} - \vec{r}) \cdot \vec{f}) \cdot \left(-1 / (4\pi^2 \vec{f}^2) \right) \times g(\vec{s}) d^2 \vec{s} \cdot d^2 \vec{f}. \quad (3)$$

In Eq. (3), $\vec{s}$ and $\vec{f}$ denote the integral variables in the coordinate space and frequency space, respectively. Hence, one can compute the phase map $\varphi(\vec{r})$ by using Eq. (2) with the help of Eq. (3). The TIE-based method is effective and fast for phase retrievals in the cases with strong phase contrast effects and low noise levels as is shown in many cases discussed in the literature.^{11,12} However, the Achilles heel of the TIE-based method lies at the inverse Laplacian operator ∇^{-2} involved in Eq. (2). The operator ∇^{-2} adds a zero-frequency singularity to Eq. (2), as is suggested by Eq. (3). As we will see below, the singularity may amplify the noise randomly embedded in the acquired images and result in instability in phase retrievals.

In order to get rid of the singular pseudodifferential operator ∇^{-2} involved in the TIE-based phase retrievals, we recently developed a novel phase retrieval method: the AP based method or the AP-based method for short.^{13,18} Our idea in this method is to utilize the correlation between the x-ray phase shift and its attenuation to eliminate any singularity involved in the phase retrievals. As is well known, in the diagnostic x-ray imaging, x-ray attenuation A_o^2 arises from three x-ray-matter interactions: the photoelectric absorption, the coherent scattering, and the incoherent scattering. Correspondingly, we can partition the x-ray attenuation into two parts: the Compton scattering-caused attenuation A_{KN}^2 and the attenuation caused by photoelectric absorption and coherent scattering, which is denoted by $A_{pe,coh}^2(\vec{r})$. That is, we can partition the overall x-ray attenuation A_o^2 into a product of two parts

$$A_o^2(\vec{r}) = A_{KN}^2(\vec{r}) \cdot A_{pe,coh}^2(\vec{r}). \quad (4)$$

The reason of factoring out A_{KN}^2 is that both of A_{KN}^2 and the phase-shift φ are determined by the tissue's electron density

$$A_{KN}(\vec{r}) = \exp \left[-\frac{\bar{\sigma}_{KN}}{2} \rho_{e,p}(\vec{r}) \right], \quad \varphi(\vec{r}) = -\bar{\lambda} r_e \rho_{e,p}(\vec{r}) \quad (5)$$

where $r_e = 2.818 \times 10^{-15}$ m is the classical electron radius, $\rho_{e,p}$, the projected electron density along the ray path, that is, $\rho_{e,p}(\vec{r}) = \int_{ray} \rho_e(\vec{r}, z) dz$, and $\bar{\sigma}_{KN}$ denotes the average Compton scattering cross-section for polychromatic x-rays. Note that Compton scattering cross-section is given by the Klein-Nishina total cross-section¹⁹

$$\sigma_{KN}(E) = 2\pi r_e^2 \left\{ \frac{1+\eta}{\eta^2} \left[\frac{2(1+\eta)}{1+2\eta} - \frac{1}{\eta} \log(1+2\eta) \right] + \frac{1}{2\eta} \log(1+2\eta) - \frac{1+3\eta}{(1+2\eta)^2} \right\}, \quad (6)$$

where $\eta \equiv E / 511$ keV and it slowly varies with x-ray energy E for $E \ll 511$ keV. We observed that the extent of the correlation between phase and attenuation depends on the x-ray photon energies and the tissues elemental compositions. For example, for light elements with atomic numbers $Z < 10$ and x-rays of 60 keV or higher, the x-ray-matter interactions are dominated by the Compton scattering, hence, both the tissue attenuation and phase shift are all determined by tissues' electron density distributions. We call this relationship between phase shift and attenuation the phase-attenuation duality, and we define the so-called duality transform as²⁰

$$\mathfrak{D}(I(\vec{r}_D)) \equiv (1 - (\bar{\lambda}^2 R_2 r_e / 2\pi M \bar{\sigma}_{KN}) \nabla^2)^{-1} \cdot \left(\frac{M^2 I(\vec{r}_D)}{I_{IN}} \right). \quad (7)$$

For the cases where the x-ray-matter interactions are dominated by the Compton scattering, we proved that the attenuation A_{KN}^2 can be found from a single phase contrast image $I(\vec{r}_D)$ by means of the duality transform such that $A_{KN}^2(\vec{r}) = \mathfrak{D}(I(\vec{r}_D))$.²⁰ With the help of the phase-attenuation duality, the phase-shift map of the object can be simply retrieved as

$$\varphi(\vec{r}) = \frac{\bar{\lambda} r_e}{\bar{\sigma}_{KN}} \ln A_{KN}^2(\vec{r}) = \frac{\bar{\lambda} r_e}{\bar{\sigma}_{KN}} \ln \mathfrak{D}(I(\vec{r}_D)). \quad (8)$$

We call this formula as the phase-attenuation duality-based phase retrieval formula.²⁰ One significant advantage of this duality-based phase retrieval formula is that the pseudodifferential operator $(1 - (\bar{\lambda}^2 R_2 r_e / 2\pi M \bar{\sigma}_{KN}) \nabla^2)^{-1}$ involved in Eqs. (7) and (8) is free of any singularity. Therefore, the phase retrieval method based on the phase-attenuation duality is stable and robust against the noise in images.²⁰

Unfortunately, the phase-attenuation duality does not hold in some other cases such as imaging with low energy x-rays or imaging bones and calcifications that contain substantial amount of heavy elements. In those cases, the retrieved phase map using Eq. (8) may provide merely coarse estimates of the real phase maps of the imaged objects. In order to overcome this limitation of the duality-based phase retrieval formula Eq. (8), recently we proposed to correct the errors iteratively through repeated comparisons of the computed estimates of the x-ray Fresnel-diffraction intensities against the acquired projection intensities. To implement this strategy, we developed the attenuation-partition based iterative algorithm, whose flow chart is shown in Fig. 1.¹³ While interested readers can find the mathematical proofs of the algorithm in Ref. 13, here, we give a brief explanation of this algorithm flow chart in Fig. 1. In this flow chart, A_o^2 denotes the attenuation map of the imaged object measured from its contact radiograph and I is the acquired phase contrast image of the object. In the flow chart, I_{KN} denotes the simulated phase contrast image formed

FIG. 1. Flow chart of the AP based iterative algorithm.

by using the estimated object's electron densities and by turning off the attenuation processes associated with x-ray photoelectric absorption and coherent scattering. In Fig. 1, two transforms are implemented in the iterations, one is the Fresnel-diffraction transform $\mathcal{F}_r$, which implements x-ray Fresnel-diffraction,²¹ and the other is the duality transform $\mathcal{D}$ as is defined in Eq. (7). According to this flow chart (Fig. 1) of the AP-based phase retrieval method, one first applies the duality transform $\mathcal{D}$ to the acquired phase contrast image I to obtain an estimate of A_{KN}^2 and the phase map ϕ of the object. One then compares A_{KN}^2 against the measured A_o^2 and computes the error $\delta A \equiv A_{KN}^2 - A_o^2$. Applying the Fresnel-diffraction transform $\mathcal{F}_r$ to the fictitious transmission function $\delta A \cdot \exp(i\phi)$, one computes the I_{KN} -correction $\delta I \equiv |\mathcal{F}_r(\delta A \cdot \exp(i\phi))|^2$, and a new estimate of I_{KN} is determined as $I_{KN} = (\sqrt{I} + \sqrt{\delta I})^2$. With this new estimate of I_{KN} , one can start a new round of the iteration as is indicated in the flow chart Fig. 1. The iteration converges when the I_{KN} does not change substantially with further iteration steps.¹³

III. COMPARISON OF THE TWO PHASE RETRIEVAL METHODS

In order to compare the robustness of above two phase retrieval methods, namely, the TIE-based method and the AP-based method, we applied the two methods for retrieving the phase map of a piece of air-bubble wrap. In the bubble wrap, the air packets are locked between two thin layers of low-density polyethylene films forming the air bubbles. Shown in Fig. 2(a) is a contact radiograph of the wrap. The x-ray source used was a micro-focus x-ray tube (L8121-02, Hamamatsu) with a focal spot size of 7 μm . The source has a tungsten target without added filtration and was operating at 40 kVp and 0.2 mA for a 30 s exposure. The average x-ray photon energy was estimated at 14.6 keV for the 40 kVp x-rays. In this acquisition, the source-detector distance (SID) was set to 1.78 m. The imaging detector employed was an aSe-based flat-panel detector (DirectRay, Hologic) with a pixel pitch of 140 μm . Since the thin polyethylene films and locked air bubbles in the wrap generate little differences in x-ray attenuation, hence, the wrap's radiograph in Fig. 2(a) exhibits only little image contrast, and the x-ray quantum noise in the acquisition

(a)

(b)

FIG. 2. (a) Contact radiograph of the bubble wrap acquired at 40 kVp and with a SID = 1.75 m. (b) Intensity profile along the marked line on (a).

masked the wrap's details such that the rims of many bubbles are not visible on the image. Figure 2(b) shows a profile of image intensities along the marked dash line on Fig. 2(a) and the profile reveals how the noisy intensity variations mask the low contrast rims of the bubbles. In contrast, Fig. 3(a) is a phase contrast image of the bubble wrap. This phase contrast image was acquired with a sample-detector distance $R_2 = 1.15$ m and otherwise the same technique settings as that used for the radiograph, that is, with the same focal spot size, same tube voltage, same tube current and exposure time, same SID, and the same detector. However, in this projection, the phase-shifted x-rays were allowed to freely diffract over 1.15-m long distance on their way to the detector and to form the interference fringes at the bubble boundaries on the image. As is shown in Fig. 3(a), the phase contrast depicts not only the bubble rims, but also the dents inside the bubble domes. The enhancement is resulted from the rapid changes of the projected thicknesses of the polyethylene films at the bubble rims and the dents inside bubble domes. These rapid changes in the projected thicknesses of polyethylene generate as well rapid changes in x-ray phase shifts, since the x-ray phase shifts are given by $\phi(\vec{r}) = -\lambda r_e \rho_e T_p(\vec{r})$, where ρ_e denotes polyethylene film's electron density and $T_p(\vec{r})$ denotes projected thickness of polyethylene along the ray. According to

FIG. 3. (a) Phase contrast image of the bubble wrap, which was acquired at 40 kVp and with a SID = 1.75 m and a magnification factor $M = 2.8$. (b) Intensity profile along the marked line on Fig. 3(a).

Eq. (1), the Laplacian and gradient differentials of the rapid phase shifts generated large x-ray intensity variations, which manifest as the bright-dark fringes flank along the bubble rims in Fig. 3(a). Figure 3(b) shows a profile of image intensities along the marked dash line on Fig. 3(a), as the line traces the same positions as indicated by the dash line on Fig. 2(a). The downward and upward overshooting of the intensity values in the profile represent the bright and dark fringes at the bubble boundaries in phase contrast image Fig. 3(a). These up-down bipolar overshootings of intensities are much larger than the background noise, hence, the noise gets masked in Fig. 3(a). While the edge-enhancement generated by phase-contrast is generally useful for imaging the wrap, however, such edge-enhancements may lead interpretation errors in the characterization of the wrap's structure and composition. For example, in Fig. 3(a), the dark fringes flanked the enhanced bubble rims may be confused with possible structural breaks in the wrap sample, although we knew in advance that this wrap sample is free of any damage. In order to fully exhibit the wrap's phase contrast and correctly characterize the bubble wrap, it is necessary to perform the phase retrieval. In order to retrieve the wrap's phase-shift map from the wrap's radiograph [Fig. 2(a)] and its phase contrast image [Fig. 3(a)], we first employed the TIE-based phase retrieval formula Eq. (2). The retrieved

phase map with the TIE-method is shown Fig. 4(a). Apparently, the phase retrieval failed completely, since no bubble is recognizable in Fig. 4(a). Although the failure can be

FIG. 4. Retrieved phase maps of the bubble wrap. (a) With the TIE-based method. (b) With the TIE-based method and Tikhonov regularization. (c) Profile of the retrieved phase values along the marked line on (b).

ascribed to the high-levels of the quantum noise presented in the radiograph of Fig. 2(a), but it is rooted in the intrinsic instability of the TIE-method. As we pointed out in Sec. II, the inverse Laplacian operator ∇^{-2} plugs in the zero-frequency singularity into the TIE-base phase retrieval formula Eq. (2). The singularity amplified the noise randomly embedded in the projections and results in the failure in the phase retrievals. To mend the instability of the TIE-method, one can try to apply the regularization techniques to tame the singularity-caused problems. A common regularization technique in the literature is Tikhonov regularization.²² With this regularization scheme, one replaces the inverse Laplacian operator ∇^{-2} by a pseudodifferential operator $\nabla^2/[(\nabla^2)^2 + \alpha^2]$, where α is the regularization parameter, which is roughly proportional to the images noise-signal ratios of the images.²² In essence, Tikhonov regularization seeks the minimum-norm, least squares solution of Eq. (2). While the Tikhonov regularization of the inverse Laplacian operator may tame the instability, it sacrifices the phase retrieval accuracies. The performance in phase retrieval of Tikhonov regularization is highly dependent on the amounts of noise presented in the images. The regularization parameter α was selected through a trial by comparing the phase maps retrieved with a wide range of α -values such as $\alpha = \Delta u^2$, $5 \Delta u^2$, $10 \Delta u^2$, $50 \Delta u^2$, $100 \Delta u^2$, $200 \Delta u^2$, $300 \Delta u^2$, and $500 \Delta u^2$, where Δu is the frequency sampling-step used in the phase retrieval. Figure 4(b) is the wrap phase map retrieved using the TIE-method and Tikhonov regularization with $\alpha = 200$ and $\Delta u^2 = 3.782 \times 10^{-8} \mu\text{m}^{-2}$, which was the α -value for the best results as determined from the trial. Apparently, these retrieval results are very unsatisfactory. In Fig. 4(b), the bubble rims are hardly visible in the extremely cluttered background. Figure 4(c) shows the profile of the retrieved phase values along the marked dash line on Fig. 4(b). As we will explain below that these phase values are grossly erroneous.

As a comparison, we have applied the AP-based method to the wrap's images in Figs. 2(a) and 3(a) for the phase retrieval as well. Following the method's iteration flow chart in Fig. 1, we succeeded in retrieving the wrap's phase map of the bubble wrap with ten iteration steps. Figure 5(a) is the retrieved phase map of the wrap with the AP-based method. In a stark contrast to Figs. 4(a) and 4(b) where the bubble rims are hardly visible, the bubble rims are prominently depicted in Fig. 5(a). A profile of retrieved phase values along the marked line on Fig. 5(a) is shown in Fig. 5(b). Note that all the marked lines in Figs. 3(a), 4(b), and 5(a), respectively correspond to the same line defined on the bubble wrap. In this way, one can easily compare the three profiles shown in Figs. 3(b), 4(c), and 5(b). In order to study the quantitative aspects of the retrieved phase maps of the wrap, remember that the amount of phase shift along a ray is given by $\varphi(\vec{r}) = -\lambda r_e \rho_e T_p(\vec{r})$, here, ρ_e denotes polyethylene film's electron density and $T_p(\vec{r})$ denotes projected thickness of polyethylene along the ray. Note that x-ray phase shifts should be of negative values, as x-ray refractive indices of tissues and materials are complex and their real part are less than one. The x-rays traversed longer paths in polyethylene at the bubble rims and incurred larger phase shifts, as

Fig. 5. (a) Retrieved phase maps of the bubble wrap with the AP-based method. (b) Profile of the retrieved phase values along the marked line on (a).

compared to other parts of the wrap. For example, the three sharp negative peaks in the profile Fig. 5(b) reflect the large x-ray phase shifts incurred at the three rim locations along the marked line in Fig. 5(a). In order to gauge the accuracies of the retrieved phase values profiled in Fig. 5(b), one has to know the values of $T_p(\vec{r})$, the projected thicknesses in polyethylene films. Apparently, $T_p(\vec{r})$ depends on the local curvatures of bubble domes and the incident angles of the rays. While it is hard to measure $T_p(\vec{r})$ values in the bubbles, we measured the thicknesses of the flat bases between bubbles using a caliber ruler, and we found that the base thickness was about 0.055 mm. Knowing that the molecular formula of the low-density polyethylene film is $(\text{C}_2\text{H}_4)_n$ and its mass density is 0.925 g/cm^3 , we calculated its electron density as $3.18 \times 10^{23}/\text{cm}^3$. Assuming approximately all rays have normal incidence, we find that the approximate phase shifts at the flat bases between bubbles is about -4.2 radian. On the other hand, according to the phase profile in Fig. 5(b), the average phase shift at the flat bases between bubbles is -1.05 radian. Obviously, these two estimates of the phase values though different, but are reasonably close. In comparison, the phase profile in Fig. 4(c), which was obtained by using the TIE-based method with Tikhonov regularization, depicts just messy up-down peaks buried in cluttered and

noisy background. In the phase profile, Fig. 4(c) only two negative peaks at the rims are barely recognizable, and the third expected negative peak completely disappears. According to this profile, the phase-shift values at the bases fluctuate over a wide range from 0 to +87.5 radian with an average of +27.3 radian, while x-ray phase shifts should be negative. Hence, the average phase value of flat bases estimated based on the profile, Fig. 4(c) is in a gross discrepancy with the thickness measurement-based estimate. Therefore, the above comparisons show clearly that the AP-based phase retrieval method is shown to be superior to the TIE-based method, regardless if the Tikhonov regularization is used, in performing the phase retrieval for the bubble wrap.

Before ending this section, we want to demonstrate the usefulness of performing the phase retrieval for tissue and material characterizations by comparing the bubble wrap's phase map in Fig. 5(a) to its phase contrast image in Fig. 3(a). As we pointed out earlier, the dark fringes which are flanking the bubble rims in the phase contrast image Fig. 3(a), may be confused for indicating possible structural breaks in the bubble wrap. In contrast to Fig. 3(a) riddled with the dark fringes, the retrieved phase map Fig. 5(a) does not present any dark fringes at all. This observation is also verified by comparing the phase profile Fig. 5(b) to the intensity profile Fig. 3(b). The up-down bipolar overshootings appearing in Fig. 3(b) disappear in the phase profile Fig. 5(b), where only sharp downward peaks present for depicting the large phase shifts at the bubble rims. Therefore, the wrap's phase map Fig. 5(a) clarifies the nature of the dark fringes in Fig. 3(a) such that these dark fringes do not indicate any structural break in the wrap sample.

IV. DISCUSSION AND CONCLUSIONS

This study demonstrates that the robustness against noises of a phase retrieval method is critical for the qualities of the retrieved phase map. Specifically, the striking differences between the retrieved phase maps in Figs. 4(a) and 4(b), and Fig. 5(a) underline the importance of removing the zero-frequency singularity that is intrinsic to the TIE-based method. While the TIE-based phase retrieval method is computational effective for the cases with strong phase contrast effects and low noise levels,^{11,12} it completely failed in retrieving the phase map of the bubble wrap, as is shown in Figs. 4(a) and 4(b). This is because the noise problem is especially challenging for the case at hand, as the bubble wrap has very low attenuation contrast and only moderate x-ray exposures were applied in bubble image acquisitions. From mathematical viewpoint, the TIE-based phase retrieval formula Eq. (2) is ill-posed, since it involves the inverse Laplacian operator ∇^{-2} that owns a zero-frequency singularity. Beyond the mathematics formality, this zero-frequency singularity reflects the fact that the phase contrast projection is insensitive to the slow variations of x-ray phase shifts. Seeking to recover the phase shifts by comparing the two projection images contaminated with noise, the TIE-based method has amplified the noise in retrieving the slowly varying phase shifts and ruined the phase retrieval completely. The Tikhonov regularization mends the singularity problem by replacing the inverse Laplacian operator ∇^{-2} in

Eq. (2) by a pseudodifferential operator $\nabla^2/[(\nabla^2)^2 + \alpha^2]$ with a regularization parameter $\alpha^2 > 0$. As is shown in Fig. 4(b), this regularization made some but only little improvement compared to Fig. 4(a) as the bubbles start to appear in the phase map but are still hardly visible. From the mathematical formulation of the Tikhonov regularization technique, it is clear that Tikhonov regularization just limits the overall magnitude of the errors caused by the noise in the retrieved phase map, but the details of the original phase map could still get lost in the retrieval.²² The AP-based method mends the singularity problem by utilizing the correlations between x-ray attenuation and x-ray phase shifts generated by tissues or materials, as is shown in Eq. (8). In a sense, the AP-based method utilizes the object's x-ray attenuation to get rid of the low-frequency singularity and the associated noise amplification. This physics-motivated regularization scheme for the AP-based method is expected to be more effective than Tikhonov regularization in phase retrievals. The greatly improved quality of the retrieved phase map shown in Fig. 5(a), as compared to Figs. 4(a) and 4(b), validates this expectation. Hence, the performance differences of these phase retrieval methods underscore the importance of developing an effective method to remove the singularity that is intrinsic to the TIE-based method. After all, the high noise levels in the acquired images still take tolls on the quality of the phase map Fig. 5(a) retrieved the AP-method, where the noise are quite visible. While increasing radiation doses used in the projections is a possible solution for improving phase retrievals, but the radiation dose constraints are stringent in many applications. In clinical applications, it is imperative to limit and reduce radiation doses involved in the imaging. Therefore, more research is needed for developing ever-improved phase retrieval methods for future clinical applications of phase contrast imaging.

Other factors, which are less critical to the robustness of phase retrieval but may affect the accuracies of retrieved phase maps, include the detector calibrations such as the flat-field and gain corrections, and the ways to incorporate the spectral averaging effects of polychromatic x-rays. In fact, the residual background nonuniformity in the acquired images [Figs. 2(a) and 3(a)] also caused variations in the background phase values in Fig. 5 and reduced their accuracies. A careful detector calibration in future experiments should avoid this kind of problem. In addition, note that x-ray wavelength enters as an important parameter in Eq. (2) for the TIE-based method, and in the flow chart in Fig. 1 for the AP-based method. The average x-ray wavelength used in the phase retrievals should represent the wavelength's linear and nonlinear effects averaged over the exiting x-rays spectrum and the detector's spectral response. For the TIE-based method, several works discussed the ways of performing the spectral averages over polychromatic x-rays.^{8,23} We did not use these techniques in this work, because the TIE-based method in any way failed the wrap's phase retrieval. In this work, we simply use the estimated average photon energy of the incident x-ray to incorporating the spectral averaging. In the future, we may develop more elaborated ways for incorporating the spectral averaging effects. Finally, we mention that one could as well employ a special phase retrieval method for the simple samples such as the bubble wrap. This

special method works specifically for the single-material homogeneous samples, as long as the linear attenuation coefficient and refractive index of this material are provided. In this special method, the phase map of a single-material sample can be retrieved from just a single phase contrast image of the sample.²⁴ The air-bubble wrap can be approximately treated as a single-material sample as the air in bubbles contributes negligibly to x-ray attenuation and phase shifts. In this work, we do not compare this special method for single-material samples to the TIE-based and AP-based methods, since both the TIE-based and AP-based methods are the general phase retrieval methods applicable for any general objects of inhomogeneous materials.

In summary, in this work, we compared the robustness of two phase retrieval methods, the TIE-based method and the AP-based method, by analyzing the retrieved phase maps from the experimental projection images of an air-bubble wrap. We showed that the TIE-based method, regardless if the Tikhonov regularization is used, failed in retrieving the wrap's phase map. In contrast, in the wrap phase map retrieved by using the AP-based method bubbles are clearly recovered. The retrieved phase values with this method are reasonably close to the estimate based on the thickness-based measurement. The stark performance differences of the two methods are rooted in their different techniques employed to deal with the singularity problem. This comparison shows that the conventional TIE-based phase retrieval method, regardless of using Tikhonov regularization or not, is unstable against the noise in the wrap's projection images, while the AP-based phase retrieval method is shown in these experiments to be superior to the TIE-based method for the robustness in performing the phase retrieval.

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