Fast quantitative phase imaging based on Kramers-Kronig relations in space domain

YUTONG LI,1,2 CHENG SHEN,3 JIUBIN TAN,1,2 XIU WEN,1,2 MING SUN,1,2 GUANCHENG HUANG,1,2 SHUTIAN LIU,4 and ZHENGJUN LIU1,2,*

1Center of Ultra-precision Optoelectronic Instrument Engineering, Harbin Institute of Technology, Harbin 150080, China
2Key Lab of Ultra-precision Intelligent Instrumentation (Harbin Institute of Technology), Ministry of Industry and Information Technology, Harbin 150080, China
3Department of Electrical Engineering, California Institute of Technology, Pasadena, California 91125, USA
4School of Physics, Harbin Institute of Technology, Harbin 150001, China

*zjliu@hit.edu.cn

Abstract: A fast quantitative phase imaging technology based on space-domain Kramers-Kronig relations is proposed. By incorporating Kramers-Kronig relations, we acquire distributions on phase via measurements of intensity over the captured spectrum. Only using four low-resolution images, we built a microscope prototype with a half-pitch resolution of 625 nm (final effective imaging performance of 0.5 NA) and a field of view of 3.8 mm² at a wavelength of 625 nm via a 10×/0.25 NA objective. Correspondingly, the data recording time is 0.16 s, and the space-bandwidth-time product is 243.3 megapixels per second. It is worth noting that the proposed scheme requires neither mechanical scanning nor extra illumination like interferometry. Meanwhile, the reconstruction is non-iterative and object-independent. Our method provides a high-efficiency phase retrieval framework and is promising in biomedicine and dynamic observation.

© 2021 Optica Publishing Group under the terms of the Optica Open Access Publishing Agreement

1. Introduction

Wave-front reconstruction can be divided into two categories: (1) interferometry and (2) non-interference methods. Interferometry is already a relatively mature technology and has developed various branches, like electronic speckle interference [1,2], phase-shifting interferometry [3,4], digital holography [5–7], etc. In the non-interferometric methods, phase retrieval plays a vital role, which recovers complex transmittance function of the sample from some modulus data or extra prior knowledge of optical systems. During the last decades, it has been investigated quite intensively, including the earliest Gerchberg and Saxton algorithm [8,9], transport of intensity equation [10–12], differential phase contrast (DPC) [13–15], and currently popular Fourier ptychography microscope (FPM) [16–19]. Phase retrieval technology provides an effective and safe optical imaging path for biomedical samples without phototoxicity or photobleaching as in fluorescence microscopy [20], which has been successfully applied in X-ray crystallography [21], biomedicine [22], and materials science [23–25].

Recently, digital holographic microscopy in conjunction with Kramers-Kronig relations of space-domain has been proposed, which directly transforms the intensity measurements to the spatial phase variation [26,27]. Unlike off-axis holography, it achieves a 3.3- to 4-fold increase in the space-bandwidth product (SBP). Unfortunately, extensive system calibration is needed to ensure that the sample beam and oblique reference beam are located at precise positions, which can be time-/labor-intensive. To avoid this problem, the Kramers-Kronig relations were adopted in synthetic aperture imaging [28]. Therein, the pupil modulation module is realized with a
spatial light modulator (SLM) or an iris diaphragm controlled by the motorized stage. Meanwhile, sophisticated mechanical scanning is introduced as a system component, which implies that high-precision calibration and cost issues should be considered. In contrast, FPM with a low-cost commercialized LED array microscope achieves gigapixel images simultaneous with a wide field of view (FOV) and high resolution (HR). Although FPM has achieved success with static sample reconstructions, a large amount of data captured and the long iterative process still inhibit live-cell applications [29]. In DPC, two pairs of images with asymmetric illumination intensity patterns are captured to recover the quantitative phase [13]. However, the quantitative inversion method demands that the sample should satisfy the assumption of weak object approximation, which is equivalent to the first order of Taylor approximation.

In this work, we propose a fast and robust reconstruction algorithm, termed annular-illumination quantitative phase imaging based on space-domain Kramers-Kronig relations (AIKK). Generally, the central region in the Fourier spectrum always has a zero-frequency component, which can be seen as the distribution of the reference wave in the off-axis holographic spectrum. Due to the consistent relationship between the real and imaginary parts, we apply Kramers-Kronig relations to achieve data inversion and phase retrieval by capturing four low-resolution (LR) images. By stitching four sub-spectrums together, a large SBP-T of 243 megapixels per second (3.8 mm² FOV, 625 nm half-pitch resolution, and 38.9 megapixels captured in 0.16 s) is obtained. AIKK has three main advantages: firstly, the experimental requirements are simplified without reference beam and mechanical scanning. Secondly, AIKK is more robust than the other methods in terms of noise and LED fluctuation. Thirdly and most importantly, data measurement volume is drastically reduced (only four intensity patterns per reconstruction). Besides, the time complexity is minimized remarkably due to the non-iteration reconstruction. Compared with FPM, AIKK cuts down the time cost by a factor of 100 without sacrificing reconstruction quality. AIKK may provide new insights and find essential applications in pathology and real-time dynamic phase imaging.

2. Methods

2.1. Experimental setup

Figure 1(a) shows the schematic illustration of the AIKK system. It can be expediently implemented using an inexpensive hardware modification to the microscope simply by replacing the lighting source with an off-the-shelf LED array. The RGB LEDs have a narrow bandwidth (about 20 nm) around center wavelength of 625 nm, 516 nm, and 465 nm. Considering the tilt angles (NA_{ill}) in the illumination module of AIKK system, the LED elements should be located on a ring, which matches the objective numerical aperture (NA_{obj}). To achieve isotropic imaging resolution, the LEDs should be lighted up as much as possible in all directions. Typically, the LED array can be regarded as a rigid, planar illuminator, in which the spacing between two adjacent LED elements is 4 mm. We choose twelve LED elements on the board to provide annular illuminations with a radius of 20 mm, the LEDs spatial coordinates (±20 mm, 0 mm), (0 mm, ±20 mm), (±12 mm, ±16 mm), (±16 mm, ±12 mm), as shown in Fig. 1(b). Considering all the above factors, the distance between the sample and the LED matrix is set as 77.45 mm. An x-y-z motorized stage was used to fix the LED array. All images are captured by an Olympus IX73 inverted microscope including a 10×/0.25 NA objective (Olympus Plan Achromat objective) and a 16-bits scientific CMOS camera (PCO.edge 4.2 LT, 2048×2048 pixels, 6.5 µm pixel pitch, 40 fps).

Generally, the spectrum distribution obeys the brighter parts that exist around the central region and extrapolate outward in some directions, such as USAF resolution target, which has more informative measurements located along with the horizontal and vertical directions [30,31]. To further compress image acquisition and reconstruction time, turning on the LEDs on the top-bottom and left-right of annular illumination, it generalizes imaging resolution well to nearly
Fig. 1. A schematic diagram of the AIKK setup. (a) The experimental setup on an Olympus IX73 inverted microscope with a 10×/0.25 NA objective, an LED array source, and a 16-bits scientific CMOS camera. (b) Schematic of experimental setup. (c) The annular illuminations. (d) Fourier coverage via (c).

2 NA_{obj}. In this case, we experimentally measure the frame rate of AIKK system to be ~6.25 Hz for capturing four bright-field raw images (40 ms exposure time per image).

2.2. Forward imaging model

The flow chart of the algorithm is depicted in Fig. 2. Given an optically-thin sample complex value \( o(r) \), where \( r = (x, y) \) denotes the lateral coordinate in the sample plane. It is illuminated via four LEDs with spatial frequency coordinates \( k_m = (2 \pi \sin \theta_{xm}/\lambda, 2 \pi \cos \theta_{ym}/\lambda) \) for \( m = 1, 2, 3, 4 \), where \( (\theta_{xm}, \theta_{ym}) \) represents different illumination angles and \( \lambda \) is the wavelength. In the experiment, the offsets of \( k_m \) could be post-calibrated with the brightfield self-calibration by use of frequency-spectrum analysis [32]. Followed by error optimization, we can ensure the sub-pixel accurate position of each LED, which is located at the edge of the cut-off spatial angular frequency. Then the exit wave from the sample is the multiplication of two units: \( e(r) = o(r)e^{-jkr} \). \( O(k - k_m) \) corresponds to the shifted spectrum around \( k_m = (k_{xm}, k_{ym}) \) of the object. The certain sub-region in the corresponding sample spectrum is

\[
G_m(k - k_m) = O(k - k_m) P(k),
\]

where \( P(k) \) is the pupil function of the objective lens.

As the existence of the large zero-order (DC) term, each sub-spectrum \( G_m(k - k_m) \) can be equally divided into supposed sample function \( \tilde{G}_m(k) \) in Fig. 3(c1) and a delta function \( \delta(k - k_m) \) in Fig. 3(c2). The latter locates at the circle edge of sub-spectrum. By using the intensity-only image captured [33] and the frequency shift property, the same LR images are measured despite the sub-spectrum being located at the center of the Fourier plane, as shown in Figs. 3(a2) and (b2). Therefore, the process relating the transmission function to the captured LR image \( I_m(r) \) is equivalent to

\[
I_m(r) = |\mathcal{F}^{-1} \{ G_m(k - k_m) \}|^2 = |\mathcal{F}^{-1} \{ G_m(k) \}|^2 = |\mathcal{F}^{-1} \{ \tilde{G}_m(k) + \delta(k - k_m) \}|^2,
\]

where \( \mathcal{F}^{-1} \) is the 2D inverse Fourier transform operator.
Fig. 2. Flow chart of the AIKK reconstruction algorithm. (a) Block diagram illustrating the processing parts involved two subsections: forward imaging model and reconstruction algorithm based on Kramers-Kronig relations. Exemplary images (b)-(g) are provided for an experimental result at the output of every step in complex field decoding: (b) the ground truth, (c) cropped spectrums, (d) captured brightfield images, (e) the Fourier spectrums corresponding to (d), (f) definite sub-spectrum distributions of the supposed sample function, (g) stitch four sub-spectrums together, (h) reconstruction results.

Mathematically, the intensity spectrum of the captured raw image via annular illumination can be expressed as

$$F\{I_m(r)\} = \tilde{G}_m(k) \star \tilde{G}_m(k) + \delta(k) + \tilde{G}_m[-(k - k_m)] + \tilde{G}_m(k - k_m),$$

where $F$ is the 2D Fourier transform operator and “$\star$” denotes autocorrelation operator. Referring to off-axis holographic imaging, the intensity spectrum can be separated into two terms: self-interference and cross-interference.

2.3. Reconstruction algorithm based on Kramers-Kronig relations

Titchmarsh theorem [34] is to ensure equivalence between causality and wave propagation relations, and strict connection between the mathematical properties of the physics functions in time and frequency domains. The following three statements for a complex-valued function $x(t)$ are mathematically equivalent as

1. $x(t) = 0$ if $t \leq 0$ and $x(t) \in L^2$. 

2. \( x(\omega) \in L^2 \) if \( \omega \in \mathbb{R} \) and if

\[
x(\omega) = \lim_{\omega' \to 0} x(\omega + j\omega'),
\]

then \( x(\omega + j\omega') \) is holomorphic if \( \omega' > 0 \).

3. Kramers-Kronig relations [35] describe a fundamental connection between the real and imaginary parts of \( x(\omega) \) as

\[
\begin{align*}
\text{Re}[x(\omega)] &= \frac{1}{\pi} \int_{-\infty}^{\infty} \frac{\text{Im}[x(\omega')]}{\omega' - \omega} d\omega', \\
\text{Im}[x(\omega)] &= -\frac{1}{\pi} \int_{-\infty}^{\infty} \frac{\text{Re}[x(\omega')]}{\omega' - \omega} d\omega',
\end{align*}
\]

where \( P \) denotes the Cauchy principal value. \( \text{Re}[\cdot] \) and \( \text{Im}[\cdot] \) are the real-valued and imaginary-valued functions, respectively.

The causality of \( x(t) \) and its square-integrable property over the real \( t \)-axis mean that the Fourier plane of the object with an upper half aperture is analytic. The real and imaginary parts are not wholly independent but are connected by nonlocal, integral systems called dispersion relations.

We define two main functions: the supposed sample function \( S(\vec{r}) = \mathcal{F}^{-1} \{ \tilde{G}_m(k) \} \) and delta function \( D(\vec{r}) = \mathcal{F}^{-1} \{ \delta(\vec{k} - \vec{k}_m) \} \approx e^{-j\vec{k}_m\vec{r}} \) in discrete case. The Eq. (2) can be simplified as \( I(\vec{r}) = |S(\vec{r}) + D(\vec{r})|^2 \). Then, we get

\[
\frac{I(\vec{r})}{|D(\vec{r})|^2} = \left| \frac{S(\vec{r})}{D(\vec{r})} + 1 \right|^2.
\]

The logarithm of Eq. (6) is

\[
\log \left| \frac{S(\vec{r})}{D(\vec{r})} + 1 \right| = \frac{1}{2} \left[ \log(I(\vec{r})) - \log \left( |D(\vec{r})|^2 \right) \right].
\]
We define a complex function \( X = \log \left( \frac{S(\vec{r}) D(\vec{r})}{|S(\vec{r}) D(\vec{r})|^2} + 1 \right) = \text{Re}[X] + j \text{Im}[X] \). The real part of \( X \) is then converted into
\[
\text{Re}[X] = \log \left| \frac{S(\vec{r}) D(\vec{r})}{|S(\vec{r}) D(\vec{r})|^2} + 1 \right| = \frac{1}{2} \left[ \log(I(\vec{r})) - \log \left( |D(\vec{r})|^2 \right) \right]. \tag{8}
\]
According to Eq. (5), Kramers-Kronig relations conduct a contour integration to retrieve the continuous complex function. In practice, the intensity images are integrated by pixel elements of the sensor, which can be seen as a discrete sampling process. A special form of Kramers-Kronig relations termed as directional Hilbert transform \([36]\) is adopted to connect the real and imaginary parts. The contour integration can be equivalently expressed as
\[
\text{Im}[X] = -j \mathcal{F}^{-1} \left\{ \text{sgn} \left( k_\parallel \cdot k_\parallel \right) \mathcal{F} \{ \text{Re}[X] \} \right\}, \tag{9}
\]
where \( k_\parallel \) and \( k_\perp \) are two quadrature components, \( k_\parallel = k_m / |k_m| \). and \( \text{sgn}(\cdot) \) is a signum function which dominantly determined by the direction angle between \( k_m \) and \( k_\parallel \).

Eq. (8) and Eq. (9) are integrated as follows
\[
\frac{S(\vec{r})}{D(\vec{r})} + 1 = \exp \left\{ \frac{1}{2} \left[ \log(I(\vec{r})) - \log \left( |D(\vec{r})|^2 \right) \right] + \mathcal{F}^{-1} \left\{ \text{sgn} \left( k_\parallel \right) \mathcal{F} \{ \text{Re}[X] \} \right\} \right\}. \tag{10}
\]
Then we can get the spectrum distribution of four definite segments as
\[
\tilde{G}_m(k - k_m) = S \left\{ \mathcal{F} \left\{ S_m(\vec{r}) \right\} \right\}, \quad m = 1, 2, 3, 4, \tag{11}
\]
where \( S \{ \} \) is a shift operator that moves the sub-spectrums to their original positions.

Finally, the Fourier spectrum of the supposed sample function can be coalesced as
\[
\tilde{G}(k) = \frac{\sum_{m=1}^{4} \tilde{G}_m(k)}{\sum_{m=1}^{4} D(k - k_m) + \alpha}, \tag{12}
\]
where \( \alpha \) generally takes a regularization constant to ensure numerical stability.

3. Simulations

Before implementing AIKK to an actual experimental system, we validate the feasibility of the scheme by numerical simulations. Simulations are set up to match our AIKK experimental system parameters in Section 2.1. The calculation is performed in the same computer environment (Intel i7-4790k CPU @4.00GHz, 32GB DDR3 memory). Furthermore, we compare the simulated results of the proposed AIKK with the other existing techniques: (1) FPM, (2) FPM based on four images, (3) high-magnification DPC. We employ all FPM methods for unrolling 20 iterations to further ensure high temporal resolution in the simulations. Figures 4(a1) and (a2) represent input amplitude and phase profiles with \( 200 \times 200 \) pixels, which serve as ground truth for validation. Figures 4(b1)-(e1) and (b2)-(e2) show recovered amplitude and phase profiles via four methods. The FOV, resolution, and calculation time of four methods are intuitively presented in Figs. 4(b3)-(e4). To quantitatively analyze the fidelity and convergence speed of reconstruction algorithms, we utilize normalized correlation coefficient (NCC) as the evaluation criterion.

Theoretically, the reconstruction performances of the above methods are governed by the nominal 0.5 NA resolution effective imaging. There are some essential differences among them. Firstly, we utilize AIKK to achieve the same SBP as in FPM (0.5 NA resolution across a \( 10 \times \) FOV), but with simply four LR images, as opposed to 81. To make a fair comparison, we use the same data set for AIKK and FPM. It is observed that the rebuilt results are corrupted by the insufficient overlapping ratio (the spectrum overlapping percentage between two neighboring apertures at least 31.81%) of the 4-images FPM scheme \([37]\). Secondly, we exploit Kramers-Kronig relations
Fig. 4. The recovery results of the FPM, DPC, and AIKK. (a1)-(a2) The ground truth. (b1)-(e1) and (b2)-(e2) the recovery amplitude and phase via four methods. (a3) FOV of the ground truth. (b3)-(e3) Resolution, FOV, and data processing times via four methods.

To recast the super-resolution reconstruction without iteration. Compared with the iterative FPM method, the reconstruction time of AIKK is significantly compressed from 35.86 s to 0.68 s. Thirdly, similarly to AIKK, DPC also only uses four intensity images (left, right, top, and bottom half-circles) to recover quantitative phase images. Unlike DPC, AIKK neither needs to satisfy the assumption of the weak object approximation nor requires deconvolution-based processes. Moreover, the pixel of the raw intensity image captured in DPC should be at least higher than the Nyquist sampling frequency corresponding to the incoherent diffraction limit. To achieve the same resolution as AIKK, a higher magnification objective is utilized in DPC system. However, the loss of FOV is much larger than the improvement of resolution, coming at the cost of significantly suppressed SBP, as shown in Fig. 4(d2). Here, it is worth mentioning that owing to the partially coherent band limit of objective, AIKK improves upon two times cutoff-frequency resolution. Thus, AIKK has better flexibility to make a trade-off among the FOV, resolution, and time according to sample observation requirements.

Furthermore, we consider that the measured intensity images are contaminated with Gaussian noise under different standard deviation $\sigma_{\text{noise}}$. The average mean absolute error (AMAE) is defined as an evaluation criterion to quantify the noise level. In Fig. 5, we plot the amplitude and phase reconstruction accuracy of AIKK versus Gaussian noise, as compared to FPM based on various spectral regimes (4, 9, and 16 illuminations). To eliminate the phenomenon in Figs. 4(c1)-(c3), all FPM measurements must redundantly encode information such that neighboring LEDs result in 60% overlapping coverage of the sample Fourier space. Figure 6 shows recovered results under no noise and 30% Gaussian noise in detail. It can be seen that our proposed AIKK reconstructs high-resolution features only with four bright-field images. The FPM reconstruction process can be cast as a nonlinear optimization problem. Thereby its convergence and recovery quality are susceptible to perturbation. Corresponding to FPM with four illuminations, the reconstruction results are extremely volatile and easily fail even if it is noise-free. Likewise, the curves of amplitude and phase reconstruction accuracy in 9-images FPM decline rapidly.
Additionally, 16-images FPM achieves better contrast under Gaussian noise below 30%, but at the expense of time resolution. As the level of noise constantly increases, the phase image components in FPM are gradually distorted.

We further evaluate the reconstruction performance when suffering LED brightness nonuniformity. To mimic LED intensity fluctuation, each captured image is simulated by multiplying a random constant. The curves of NCC in Figs. 7(a)-(b) are utilized to evaluate the amplitude

**Fig. 5.** The reconstruction accuracy of amplitude (a) and phase (b) under Gaussian noise for AIKK and FPM based on 4, 9, and 16 images.

**Fig. 6.** Comparison between AIKK and FPM with Gaussian noise. (a) The recovery results without noise and 30% Gaussian noise via AIKK. (b)-(d) The recovery results without noise and 30% Gaussian noise via FPM based on different capture schemes.
Fig. 7. The reconstruction accuracy of amplitude (a) and phase (b) under LED intensity fluctuation for AIKK and FPM based on 9 and 16 images.

and phase reconstruction accuracy as a function of LED intensity fluctuation. Figures 8(a)-(c) are reconstruction results of three cases under 150%, 200%, and 250% intensity fluctuation. The final recovery result suffers from a significant degree of cross-talk between the phase and amplitude part of the complex field. When fluctuation is below 150%, all methods can achieve relatively stable reconstructions. Here, the error trajectories of 16-images FPM and the proposed method are almost analogous, which performs better than the final results in 9-images FPM. When the fluctuation continues to increase, the recovery results in 9-images FPM cannot be converged. Meanwhile, the NCC curves of amplitude and phase reconstruction in 16-images FPM decline rapidly to fail until 250% intensity fluctuation. On the contrary, AIKK is relatively stable to LED brightness uncertainty and show better contrast (amplitude: 0.9911, 0.9601, and 0.9265; phase: 0.9764, 0.9684, and 0.9519 for all fluctuation cases). We can safely conclude that AIKK offers more significant gains in reconstruction speed, acquisition time, and robustness than previous methods.

Fig. 8. Comparison between AIKK and FPM with LED intensity fluctuation. (a) The recovery results with LED intensity fluctuation via AIKK. (b)-(c) The recovery results with LED intensity fluctuation via FPM based on different captured schemes.
4. Experiments

To validate the performance of our method experimentally, we firstly compare the recovered results of a USAF target, as shown in Fig. 9. Figure 9(a1) presents the LR image of the resolution target corresponding to the central LED. The enlarged view of the region (500×500 pixels) inside the red box of Fig. 9(a1) is shown in Fig. 9(a2), and its close-up (140×140 pixels) is shown in Fig. 9(a3). The measured half-pitch resolution with a 10×/0.25 NA objective is element 5, group 8 (1.23 µm). Figures 9(b1) and (b2) demonstrate the recovered phase and amplitude via AIKK method with twelve captured images. The illumination condition is given in Section 2.1. Figures 9(c1) and (c2) are the reconstruction results via AIKK method with four captured images, which are vertical and horizontal pairs. The line-scan profiles from the selected position of targets in Figs. 9(b2) and (c2) are presented in Fig. 9(d). Two sets of illumination schemes have almost the same performance. The maximum resolvable measured of both can reach element 4, group 9 (691 nm half-pitch resolution). Theoretically, the resulting image from AIKK has a twice improvement in NA \(_{obj}\) with the achievable resolution 625 nm, corresponding smallest resolution element 4 in group 9. Compared with the 12-images scheme, more details and higher contrasts of elements 3 and 4 in group 9 are achieved with the 4-images scheme. Even the line in element 5 group 9 can be distinguished in Fig. 9(d). Thus we speculate that by turning on more LEDs on the edge of the circle, more overlap of high-frequency information may weaken the background noise but distort detailed information.

In addition, we also test the proposed method by biological samples. Figure 10(a1) shows the FOV of the human hemangioma slice, and (a2) demonstrates the enlarged view of the region (140×140 pixels). Figures 10(b1) are the captured four LR intensity images via inclined illuminations. The corresponding intensity spectrum distributions are illustrated in Figs. 10(b2), which could be post-calibrated by use of frequency-spectrum analysis. Figure 10(c1) is the recovered phase via DPC method. Here, the four DPC images are numerically constructed by taking the sum of single-LED images corresponding to vertical and horizontal half-circle pairs on the LED array [38]. Since the weak phase assumption required by the DPC deconvolution algorithm is not fully satisfied, the recovered phase information is interfered. Next, we compare the amplitude and phase reconstruction results using 81-images FPM and our method in Figs. 10(d1)-(d2) and (e1)-(e2). Following convention, the iteration number of FPM is set as 20. Both of them are able to achieve approximately consistent performance in amplitude reconstruction, whereas
FPM contains blur artifacts in phase reconstruction. Table 1 is the time cost of different methods by human hemangioma slice (1250×1250 pixels) shown in Fig. 10(a1). The time cost is classified into two categories, data recording time and processing time. On the whole, due to few captured images and non-iterative characteristics, AIKK is the least time-consuming.

![Experimental results of a human hemangioma slice.](image)

**Fig. 10.** Experimental results of a human hemangioma slice. (a1) The full FOV captured with a 10×/0.25 NA objective. (a2) The corresponding magnified areas. (b1) The captured LR intensity images. (b2) The intensity spectrum corresponding in (b1). (c1) The recovery phase via DPC. (d1)-(d2) The recovery amplitude and phase via 81-images FPM. (e1)-(e2) The recovery amplitude and phase via AIKK.

<table>
<thead>
<tr>
<th>Methods</th>
<th>Data recording time (s)</th>
<th>Processing time (s)</th>
<th>Total (s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>DPC</td>
<td>3.24</td>
<td>1.56</td>
<td>4.8</td>
</tr>
<tr>
<td>FPM</td>
<td>3.24</td>
<td>406.74</td>
<td>409.98</td>
</tr>
<tr>
<td>AIKK</td>
<td>0.16</td>
<td>2.97</td>
<td>3.13</td>
</tr>
</tbody>
</table>

To demonstrate the accuracy of the quantitative phase imaging for AIKK, we test unstained mouse neuroglial cells. Figure 11(a) is the phase recovery results via AIKK with 0.5 NA resolution. Two zoom-in phase reconstruction regions via AIKK are shown in Figs. 11(b) and (c), together with the results from the DPC and FPM methods by the same measurements. FPM gets a blurry phase recovery result. The central LR intensity image is generally used as the initial intensity guess. However, the pure phase sample cannot provide a good starting point. In addition, the reconstruction effect of FPM entirely is governed by the illumination angles, which are close to the objective NA. Due to the phase transfer function based on the weak object approximation [39,40], low-frequency information is worse to reconstruct than high-frequency information, opposed to the intensity reconstruction in FPM. Our method has almost the same quality as DPC, and both achieve the 0.5 NA resolution with high-frequency details (e.g., subcellular profile and filopodia). Additionally, we test the time cost of different
methods by unstained mouse neuroglial cells (1000×650 pixels), but consistently AIKK takes the least time, as shown in Table 2. Therefore, we confirm the ability of AIKK to compress data capacity without compromising reconstruction performance, thereby improving the temporal resolution of system without sacrificing FOV or resolution.

![Image](image-url)

**Fig. 11.** Experimental results of unstained mouse neuroglial cells. (a) The phase reconstruction with a 10× objective and achieving 0.5 NA resolution. (b) The recovery phase of the same segment (yellow rectangle, 200×200 pixels) via DPC, 81-images FPM, and AIKK. (c) The recovery phase of the same sub-region (red rectangle, 200×200 pixels) via DPC, 81-images FPM, and AIKK.

<table>
<thead>
<tr>
<th>Methods</th>
<th>Data recording time (s)</th>
<th>Processing time (s)</th>
<th>Total (s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>DPC</td>
<td>3.24</td>
<td>0.85</td>
<td>4.09</td>
</tr>
<tr>
<td>FPM</td>
<td>3.24</td>
<td>102.17</td>
<td>105.41</td>
</tr>
<tr>
<td>AIKK</td>
<td><strong>0.16</strong></td>
<td><strong>1.19</strong></td>
<td><strong>1.35</strong></td>
</tr>
</tbody>
</table>

It is worth mentioning that in order to further attain higher resolution, we need the illuminations with more oblique and the objective with higher NA. Then the noise caused by LED weak intensity, the calibration of condenser and the balance of SBP cannot be ignored. This is an important issue that we need to break through in the future work.

5. Conclusion

We presented a quantitative phase method named AIKK. This is accomplished by citing Kramers-Kronig relations to combine measurements captured by an LED array microscope with programmable annular-illumination source patterns. The synthetic aperture spectrum is expanded nearly twice by four LR images corresponding to four tilted illuminations matching a 10×/0.25 NA objective. AIKK system improves upon the resolution and achieves the final effective imaging performance of 0.5 NA, corresponding to a half-pitch resolution of 625 nm at a wavelength of 625 nm across a wide FOV of 3.8 mm². For every captured raw image with a 40 ms exposure, AIKK enhances the maximum frame rate to 6.25 Hz. Implementation of AIKK is easy, requiring only an inexpensive LED array source attachment for a commercial microscope,
substituting double beams like off-axis holography. Besides, AIKK does not need any knowledge of optional priors like DPC. Simulation and experimental results have verified that AIKK works well for both amplitude contrast imaging and quantitative phase imaging applications. Unlike FPM, the total number of required measurements in AIKK can be significantly decreased by 20 times. More importantly, AIKK is iteration-free that dramatically compressed data processing time. Further, AIKK performs higher robustness in noise and fluctuation than FPM based on the same spectrum distribution. AIKK enables high-throughput and fast-speed imaging for applications in pathological diagnosis, personalized genomics, and stem cell research.

**Funding.** National Natural Science Foundation of China (11874132, 61975044, 12074094); Interdisciplinary Research Foundation of HIT (IR2021237).

**Disclosures.** The authors declare no conflicts of interest.

**Data availability.** Data underlying the results presented in this paper are not publicly available at this time but may be obtained from the authors upon reasonable request.

**References**


