Research article

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High-efficiency, large-area lattice light-sheet generation by dielectric metasurfaces

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Abstract: Lattice light-sheet microscopy (LLSM) was developed for long-term live-cell imaging with ultra-fine three-dimensional (3D) spatial resolution, high temporal resolution, and low photo-toxicity by illuminating the sample with a thin lattice-like light-sheet. Currently available schemes for generating thin lattice light-sheets often require complex optical designs. Meanwhile, limited by the bulky objective lens and optical components, the light throughput of existing LLSM systems is rather low. To circumvent the above problems, we utilize a dielectric metasurface of a single footprint to replace the conventional illumination modules used in the conventional LLSM and generate a lattice light-sheet with a ~3-fold broader illumination area and a significantly leveraged illumination efficiency, which consequently leads to a larger field of view with a higher temporal resolution at no extra cost of the spatial resolution. We demonstrate that the metasurface can manipulate spatial frequencies of an input laser beam in orthogonal directions independently to break the trade-off between the field of view and illumination efficiency of the lattice light-sheet. Compared to the conventional LLSM, our metasurface module serving as an ultra-compact illumination component for LLSM at an ease will potentially enable a finer spatial resolution with a larger numerical-aperture detection objective lens.

Keywords: field of view; illumination efficiency; lattice light-sheet microscopy; optical metasurface; spatial frequency manipulation.

1 Introduction

Light-sheet fluorescence microscopy (LSFM) has emerged as a powerful technique for ultra-fast 3D imaging acquisitions of live samples with high spatial and temporal resolutions, low photo-toxicity and weak background noise [1–6]. LSFM has a great impact in the fields as diverse as developmental and cell biology, anatomical science and neuroscience [7–9]. In LSFM, a sample is illuminated with a thin light-sheet by an excitation objective lens from the side, and the emitted fluorescent light from the sample is captured by a perpendicularly oriented detection objective lens. The LLSM developed by Eric Betzig and his collaborators exploits a thin light-sheet with lattice patterns for illumination and is regarded as an advanced scheme of LSFM [10, 11]. Compared to other types of light-sheet illumination, the lattice light-sheet enables simultaneous optimization of axial resolution (influenced by the thickness of the light-sheet), the field of view (the effective illumination area of the light-sheet) and background noise caused by out-of-focus fluorescence excitation [12, 13]. However, there are two major drawbacks of LLSM from our point of view: expensive and complicated optical setups, as well as the inevitable trade-off between a large field of view and high light throughput. Unfortunately, Eric Betzig’s LLSM has ultra-low light throughput and there is only ~0.1–1% of the input laser power delivered to the sample [10]. Recently, a field synthesis theorem is proposed by Reto Fiolka et al. to realize the lattice light-sheet with a half less complexity and a ~15-fold increased light throughput than Eric Betzig’s LLSM system [14]. With the field synthesis, an identical time-averaged lattice light-sheet can be obtained by scanning a line-focused laser beam over the same pupil function as that in Eric Betzig’s LLSM.

The lattice light-sheet is the diffraction patterns of several light lines incident at the pupil of the excitation objective lens. Hence, the lattice light-sheet at the focal
plane of the objective can be considered as the Fourier transform of the light lines at the pupil. A broader field of view i.e. the coverage area of the lattice light-sheet extends in a transverse direction requires narrowing span range of the wave vector in that direction. Thus, the width of the light lines should be thinner in the corresponding direction which dramatically blocks the light transmission power. This is why the highly efficient lattice light-sheet generation is so challenging. In Eric Betzig’s LLSM these narrow light lines are produced by the first-order diffraction of the light from a spatial light modulation (SLM). Unfortunately, the diffraction efficiency is very limited and a large amount of the input laser power is lost before delivering to the sample. In the field synthesis LLSM, the narrow light lines are generated by step-scanning a line-shaped laser beam across the back pupil plane of an objective lens. Here is a question: are the narrow light lines at the pupil indispensable factors for the generation of lattice light-sheet? They are inevitable in the cases of the conventional objective lens and optical components. However, it is fascinating that we found it is not the case for metasurfaces.

Metasurfaces, composed of delicate arrangements of optical nano-antennas, enable effective steering and manipulation of light waves [15–19]. Unlike traditional bulky optical components, such as lenses and SLMs, precise subwavelength phase and amplitude manipulation by planar metasurfaces provides many unprecedented advantages for exploring new optical physics [20–22]. The versatile functions of metasurfaces have led to a fruitful work of many novel nanophotonics devices [23–25]. However, there seems to be a lean investigation of spatial frequency manipulation based on metasurfaces. Due to the flexible design for phase profile, metasurfaces can be a superior alternative to the lenses, prisms, or SLMs in achieving complex spatial frequency manipulation for beam steering [26–28].

Herein, we demonstrate the generation of lattice light-sheet by an ultrathin dielectric metasurface consisting of delicately aligned resonant nano-antennas. Unlike the conventional objective lens, the metasurface has the freedom of independent control of spatial frequencies in orthogonal directions, to break the limitation of illumination efficiency due to the trade-off between the thickness of light lines at the pupil and the spatial span of the resulted lattice light-sheet. Consequently, instead of currently available complex optical manipulation, solely a single metasurface with an incident collimated and expanded light beam is sufficient for lattice light-sheet generation. Furthermore, our simulations show that metasurface can surpass the conventional objective lens in another aspect. For conventional optical configuration, extremely narrow light lines at the pupil of the objective lens still lead to certain spans of the spatial frequency along the light-sheet dithering direction for the reason of line extension. However, metasurface can diminish such an unwanted spatial frequency span due to its absolutely independent phase control. According to our simulations, the illumination area of lattice light-sheet generated by metasurface (i.e. the temporal resolution of LLSM) is ~3-fold larger than that by conventional optical setup, meanwhile, the same spatial resolution of LLSM is maintained, which break another well-known key trade-off between the field of view and the spatial resolution in LSFM. Our demonstrations will promote to construct a highly integrated, ultra-compact, mechanically stable, and user-friendly LLSM with an elaborate illumination scheme based on a dielectric metasurface.

2 Theory and methods

We start with a detailed discussion on the underlying reasons why the lattice light-sheet generation is challenging with a traditional objective lens. The lattice light-sheet in an LLSM system arises out of diffraction of all the light waves near the focal plane of the excitation objective lens [29]. The diffraction pattern is the Fourier transform of the light waves incident on the lens. Thus, a desired lattice light-sheet can be obtained by delicately manipulating the spatial frequencies of the incident light waves on the excitation objective lens. First, we investigate the properties of spatial frequency manipulation by a conventional lens. As shown in Figure 1A, a lens with a focal length f is located in the xz plane at y = 0. A collimated laser beam incident on the lens is refracted and converges to the focal point at (0, f, 0). In the input xz plane, a light wave at (x, 0, z) will contribute a wavefront with spatial frequency (k_x, k_y, k_z) at the focal point, where k_i (i = x, y, z) represents the i component of the wave vector k_0 of the refracted light wave. According to the geometric relation between k_i and k_0 in Figure 1A, we have

\[ k_x = k_0 x / \sqrt{x^2 + z^2 + f^2}, \quad k_y = k_0 f / \sqrt{x^2 + z^2 + f^2}, \]
\[ k_z = k_0 z / \sqrt{x^2 + z^2 + f^2} \]  

(1)

In the spatial domain, a light-sheet should extend in the x-y plane and, in the meantime, be confined in the z-direction. Accordingly, in the spatial frequency domain, the spans of k_x and k_y should be confined and k_z needs to extend as much as possible. From Equation (1), one can note that k_y is only related to ρ (ρ^2 = x^2 + z^2). A tiny Δρ
wcorresponds to a small variation of $k_y$. Hence, the light-sheet is generally produced with the focusing of a laser beam after passing through a narrow annulus. A narrower annulus will lead to a wider extent of the light-sheet in $y$. If we assume the annulus is extremely narrow, $\rho$ will approximately be a constant. Then, the span of $k_x$ (or $k_z$) in the spatial frequency domain only depends on the spatial variation range of the light in the pupil plane of the lens in $x$ (or $z$). As discussed above, $k_x$ is required to be confined and $k_z$ extend. Therefore, the light in the pupil plane of the lens should be very narrow in $x$ with a tiny spatial variation range of $\Delta x$ but wide in $z$ with a large spatial variation range of $\Delta z$.

Figure 1B–E demonstrate the generation of light-sheets with square lattices, one type of the lattice interference patterns typically used in LLSM. Figure 1B and C show the light lines with different line widths at the pupil plane of the excitation objective lens. Figure 1D and E are the simulated $xz$ and $yz$ cross-sectional intensity distributions of the corresponding generated lattice light based on the diffraction theory using Matlab. In these two simulations, the input laser beam is a plane wave and then filtered by two opaque masks with specifically designed apertures before the beam is focused by the lens. The apertures on the masks have the same shape and size as the light lines shown in Figure 1B and C, respectively. The spatial phase profile of the lens is set as

$$\varphi(x, z) = \frac{2\pi}{\lambda} \left( \sqrt{\rho_{\text{out}}^2 + f^2} - \sqrt{x^2 + z^2 + f^2} \right)$$

where $\lambda$ is the incident light wavelength and is set as 560 nm which is the excitation wavelength of one of the widely used labeling fluorophores mCherry. $\rho_{\text{out}}$ is the outer radius of the annulus as shown in Figure 1B. The NA of the objective lens is restricted in the range of 0.5–0.6 corresponding to the annulus marked with dashed circles in Figure 1B and C with an inner radius of $\rho_{\text{in}}$ and an outer radius of $\rho_{\text{out}}$, respectively. The middle light lines are at the position of $x = 0$ and the other neighboring lines are at $x_c = \pm f \times \tan(\arcsin(\text{NA}_{\text{side}}))$, where the $\text{NA}_{\text{side}}$ is set as 0.51 corresponding to the radius from the center of the annulus to the center of the rightest light line.

Comparing the simulated results in Figure 1D and E, one can have an intuitive understanding of the influence of the width of the light lines $\Delta x$ in the pupil plane of the objective lens on the spatial coverage range of the resulted lattice light-sheet in $x$. It should be noticed that the effective illumination area of the lattice light-sheet should have a perfect interference square lattice which excludes the distorted patterns aside. In Figure 1B the width of the
light lines $\Delta x$ is set as 0.05$\rho_{\text{out}}$, and the corresponding lattice light-sheet in Figure 1D has an effective illumination field of $\sim 10 \mu m$ in $x$. The width of the light lines $\Delta x$ in Figure 1C is 0.15$\rho_{\text{out}}$ and the corresponding lattice light-sheet in Figure 1E has an effective illumination field of $\sim 6 \mu m$ in $x$. It is found that the illumination field extension in $x$ decreases as the width of the light lines becomes broader, while the length of the lattice light-sheet along $y$ changes very slightly. Hence, to obtain a possibly large illumination field in $x$, the width of the light lines $\Delta x$ in Figure 1C is 0.15$\rho_{\text{out}}$ and the corresponding lattice light-sheet in Figure 1E has an effective illumination field of $\sim 6 \mu m$ in $x$. It is found that the illumination field extension in $x$ decreases as the width of the light lines becomes broader, while the length of the lattice light-sheet along $y$ changes very slightly. Hence, to obtain a possibly large illumination field in $x$, the width of the light lines $\Delta x$ is supposed to be as narrow as possible. Therefore, there exists a trade-off between a large field of view (i.e. a high temporal resolution) and a high light throughput for the LLSM based on convention complicated illumination component.

To overcome the above limitation, one needs to break the radial symmetry of the phase distribution of a spherical lens and manipulate the spatial frequencies $k_x$ and $k_z$ independently, as sketched in Figure 2A. The linear phase profile in the $x$-direction gives rise to a constant value of $k_x$ and the parabolic profile in the $z$-direction provides a finite span of $k_z$. To obtain such phase profile with traditional bulky glass-based optical components for which the phase accumulation relies on the optical-path, one needs to combine a triangular prism which generates a linear phase profile in the $x$-direction and a semi-cylindrical lens with a parabolic phase profile in the $z$-direction, as depicted in Figure 2B. However, such a prism-lens combination suffers from a limited NA because a large NA will induce an even smaller working distance for this combination than that of a single lens.

Herein, we show that these problems can be solved by using ultrathin planar metasurfaces with flexible phase manipulation and the schematic view of the comparison between the conventional optical setup and our metasurface is depicted in Figure 2B. Our metasurface is based on the Pancharatnam-Berry (PB) phase method, for which the local phase of each unit cell is controlled by the rotation angle of the element. The incident circularly polarized light can be partly converted into inversed circularly polarized light that has the geometric phase according to the PB phase method [30–34]. Figure 2C shows a side view of the metasurface consisting of GaN nanopillars with length $L = 250 \text{ nm}$, width $W = 80 \text{ nm}$, height $H = 600 \text{ nm}$, and pitch $P = 280 \text{ nm}$. These geometrical parameters of the GaN nanopillars are optimized for the polarization conversion efficiency at $\lambda = 560 \text{ nm}$ with a complete $2\pi$ phase coverage at the same time by using the parameter sweep function of the Finite-Difference Time-Domain (FDTD) method. Typically, the values of $L$, $W$, and $H$ should be accordingly smaller for a shorter operation wavelength [35]. The complete $2\pi$ phase coverage could be achieved within a relatively broadband wavelength region due to the property of the PB phase. GaN is chosen because it has a relatively high refractive index and low losses in the visible range, and its fabrication cost is also less than other materials such as

![Figure 2](image-url)
TiO$_2$ [35–38]. For a right circularly polarized incident light beam, the phase shift of the transmitted light with the reversed polarization state can be controlled by rotating the nanopillar in the $xz$ plane along the $y$-axis. Figure 2D shows the transmittance and phase shift of the transmitted light as a function of rotation angle $\theta$. Due to the accurate control of the structure orientation, such metasurface can implement the same phase manipulation as the conventional prism-lens system. As a proof of concept demonstration, we will use such unique ability of phase manipulation in orthogonal directions based on metasurfaces for generating the lattice light-sheets in the following section.

3 Results and discussion

As shown in Figure 3, our designed metasurface produces almost identical light-sheet to that in Figure 1D, except that there are some intensity-enhanced distorted side lobes in the lateral direction at the boundary of the pattern. The diffracted light waves by the metasurface blocks, as shown schematically in Figure 3A, are overlapped on the focal plane and interfere with each other. It can be noted that the original narrow light lines in Figure 1B are replaced by metasurface blocks, depicted in Figure 3B, which have the same lengths along $z$ with that of the previous light lines but much broader widths in $x$. However, such broader widths in $x$ do not lead to the broadening of the spatial frequency in $k_x$ due to a constant phase slope of the metasurface blocks along $x$. By tailoring the orientation angle of the GaN nanopillars $\theta$, linear phase profiles in $x$ and parabolic profiles in $z$ are imposed on the metasurface. To reproduce the square lattice light-sheet in Figure 1D, the linear profiles along $x$ should satisfy

$$\varphi_x(x, z) = k_x(x_c, z)(x_c - x)$$  \hspace{1cm} (3)

where $x_c$ is the center position of each metasurface block in $x$, and $k_x(x_c, z)$ is a constant slope of the phase profile, which is equal to the $k_x$ of the original light lines in Figure 1A. The parabolic profiles along $z$ should satisfy

$$\varphi_z(z) = \frac{2\pi}{\lambda} \left( \sqrt{r_{out}^2 + f^2} - \sqrt{r_{out}^2 + z^2 + f^2} \right)$$  \hspace{1cm} (4)

where $\varphi_z(z)$ is also identical to the phase profile of the original light lines in $z$ in Figure 1B. The phase at the position $(x, z)$ should be

$$\varphi(x, z) = \varphi_x(x, z) + \varphi_z(z)$$  \hspace{1cm} (5)

The field patterns are calculated by the FDTD method implemented in a commercial full-wave simulation software Lumerical. The meshes in $x$ and $z$ over the entire simulation domain are set as 40 nm; the mesh size in $y$ is 100 nm for the GaN nanopillars and 10 nm for the metal film. Two light sources with orthogonal polarization and a 90° phase difference are set to produce a right circularly polarized incident light. Perfectly matched layer (PML) absorbing boundaries are used in all directions. A 3D projection function farfieldexact3d is used to calculate the diffraction patterns at the focal planes. For all the designed metasurfaces in this work, the radius is set as $r_{out} = 120 \times P = 33.6 \mu m$ which corresponds to an outer $NA$ of 0.6, and the spatial span width of each metasurface block in $x$ is set as $r_{out} \times 3/4 = 90 \times P = 25.2 \mu m$. The focal length of the metasurface $f = r_{out}/\tan(\arcsin(0.6)) = 44.8 \mu m$. The light is blocked by the black area in Figure 3B, which is coated with a metal film leaving the apertures transparent to the metasurface blocks.

At the focal area, the diffracted light waves from the metasurface have the same wavevector components $k_x$, $k_y$, $k_z$ as that of the light lines focused by the conventional objective in Figure 1B. Hence, the lattice light-sheet in Figure 3C is almost identical to the interference pattern in Figure 1D. The relatively stronger intensity of the distorted patterns in the $x$ direction in Figure 3C is caused by a less localized distribution in $x$. The less homogenous field
along y than that in Figure 1D is mainly due to a limited width of the metasurface blocks.

As discussed in Eric Betzig’s LLSM, the lattice light-sheet is generated from demagnifying the lattice pattern on an SLM onto the sample plane. The corresponding energy losses of the excited laser beam mainly come from the diffraction losses of the SLM. The laser energy is lost when the zero- and higher-order diffraction modes are filtered out by an annular ring mask. Thus, only \( \sim 0.1\% \) of the input laser power can be delivered to the sample. In contrast, for the lattice light-sheet generation by our proposed metasurface as demonstrated above, the losses are governed by the diffraction and the total transmission of the light from the metasurface blocks. If the size of the input laser beam is adjusted to match that of the metasurface blocks, the generation efficiency is the focusing efficiency of the metasurface blocks normalized to the ratio of the metasurface blocks area and the transverse cross-section area of the input beam. Recent developed dielectric metasurfaces have demonstrated the efficient beam steering with a high NA [39–42]. According to an experimental study of GaN metalens with NA = 0.78, an average focusing efficiency of 79% can be realized within the band of 450–660 nm [41]. Thus, we estimate a generation efficiency of \( \sim 37\% \) for the metasurface method in Figure 3, which is comparable to the transmission of 35.4% by the field synthesis LLSM in the square lattice mode [14].

Figure 4 shows an additional advantage of metasurface in lattice light-sheet generation. One can note that even the light lines in Figure 1B are extremely narrow; the spatial extension of the corresponding light-sheet along x is only \( \sim 10 \) μm. This indicates that a span of \( k_x \) still exists. Since the light lines are already quite narrow, such a \( k_x \) span is not caused by the spatial extensions of the light lines in x but originates from the finite lengths of the light lines in z. This can be perceived in Equations (1) and (3) where \( k_x \) is also a function of z. Similarly, the diffracted light waves near the focal area shown in Figure 3A also suffer from a non-negligible span of \( k_x \). We further utilize the absolute independent phase manipulation ability of the metasurface to address such a problem. To suppress such a \( k_x \) span, we can deliberately and manually set the phase profile slope of the lateral metasurface block to be a certain fixed value and unrelated to z position. Considering the diffracted light waves from the metasurface blocks from horizontal and vertical directions should overlap each other to interfere near the focal area, \( k_x \) is set to \( k_x(x_c, 0) \). Instead of the phase profile in x described in Equation (3), new linear phase profiles along x for the lateral metasurface blocks are defined as

\[
\varphi_x(x) = k_x(x_c, 0)(x_c - x)
\]  

where \( k_x \) is only related to \( x_c \) (the center position of each lateral metasurface blocks in x). Then, the phase value of the metasurface unit at \((x, z)\) should be \( \varphi(x, z) = \varphi_x(x) + \varphi_z(z) \), where \( \varphi_z(z) \) is described by Equation (4). Figure 4A shows an intuitive understanding of the diffracted light waves from such metasurface blocks. The diffracted light waves do not entirely overlap when they arrive in the focal area, but they have almost identical \( k_x \). Consequently, the resulted lattice light-sheet is expected to be much broader in x than those in Figure 1D and Figure 3C. The lattice light-sheet pattern generated by the metasurface in Figure 4B is shown in Figure 4C with an extension of over \( \sim 20 \) μm along x, which is \( \sim 3 \) times of that in Figure 3C. To the best of our knowledge, such an effective spatial broadening of the lattice light-sheet in x is firstly presented. In addition, the width of the lattice light-sheet along the x direction in Figure 4C can increase accordingly with the size of metasurface blocks in x. The practical illumination area can be enlarged much more times with larger-sized metasurface blocks.

In LLSM, square lattice light-sheet is the most widely used lattice with reduced sidelobes for excellent confinement but a thick main lobe. If a higher axial resolution is required, one may need a hexagonal lattice light-sheet with a thinner main lobe but stronger sidelobes than that of the square lattice form [10]. Here we further demonstrate the hexagonal lattice light-sheets. When \( |x_c| < \rho_{\text{im}} \), the original two light lines in the horizontal direction are separated into four lines, separately. Hence there are totally six light lines. Figure 5A demonstrates the six light lines at the pupil plane with a small \( x_c \) (\( NA_{\text{side}} = 0.49 \)). The corresponding resulted hexagonal lattice light-sheet is shown in Figure 5B. The simulation parameters are the same as those used in Figure 1B except that the \( NA_{\text{side}} \) is changed to 0.49. Figure 5C depicts the corresponding metasurface blocks with phase profiles defined as Equation (6). The simulation parameters are the same as those used in Figure 4B except that the \( NA_{\text{side}} \) is changed to 0.49. The comparison between the field distributions of Figure 5B and D exhibits a much broader light-sheet based on the metasurface rather than the conventional scheme. It can be noted in Figure 5E that the length of the illumination field along y slightly decreases in case of the metasurface-based generation in Figure 5D compared to the conventional method in Figure 5B. Nevertheless, the overall illumination area is still enlarged by using the metasurface-based method. These results demonstrate the universal effectiveness and superiority of the metasurfaces in lattice light-sheet generation.
Figure 4: (A) Schematic view of the diffracted light waves from the metasurface blocks with spatial phase profiles in (B). (B) Spatial phase profiles of the metasurface blocks are defined by Equation (6). (C) Simulated $xz$ and $yz$ cross-sectional intensity distribution of the produced square lattice light-sheet.

Figure 5: (A) Pupil function for the generation of hexagonal lattice light-sheet by the conventional LLSM, and the corresponding $xz$ and $yz$ cross-sectional intensity distribution is shown in (B). (C) Metasurface design with the same parameters used in Figure 4 except that $NA_{side} = 0.49$, and (D) the corresponding simulated $xz$ and $yz$ cross-sectional intensity distribution of the metasurface-based hexagonal lattice light-sheet. (E) The intensity profiles along $y$ at $z = 0$ extracted from the $yz$ cross-sectional intensity distributions in (B) and (D).
4 Conclusion

In conclusion, we demonstrate an effective lattice light-sheet generation utilizing metasurfaces with a specific phase design. Compared to the lattice light-sheet generation by traditional LLSM systems, our proposed metasurface method promises a ~3 times larger field of view, a much higher generation efficiency, as well as ultra-compactness of the component. The metasurfaces uphold advantages over conventional optical illumination components especially for generations of structured lattice illuminations. Our methodology opens an avenue for applications of metasurfaces in the fields of light microscope imaging and other potential technics, for instance, LLSM, optical trapping, optical lithography and et al. And it is proved to be promising next-generation on-chip photonic components especially for generations of structured lattice light illuminations.

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