

SUPPLEMENTARY TEXT and FIGURES

SUPPLEMENTARY TEXT

S1. Spatial sampling requirements at the detector plane

To complement the arguments made in the Appendix of the main text, the required pixel size (Δx_D) at the detector plane for accurate sampling of the cell holograms can be obtained by considering the spatial frequency bandwidth of each cell hologram. Using Eqs. 3-4 of the Appendix for a narrow enough $p(-x_D M, -y_D M)$, based on the Nyquist sampling theorem³⁶, one can derive the following spatial sampling requirement at the detector (assuming $n=1$; cell width L_C ; cell hologram width L_H):

$$\frac{1}{\Delta x_D} \geq \frac{(L_C + L_H)}{\lambda_0 \Delta z} = \frac{(L_C + L_H)z_1}{\lambda_0 (z_1 + z_2)z_2} \quad \text{or} \quad \Delta x_D \leq \frac{\lambda_0 z_2}{(L_C + L_H)} \cdot F \quad (\text{S1})$$

According to Eqs. 3-4 of the Appendix, each scattering point within the cell body diffracts coherently with respect to the background light over a distance of $\Delta z = (z_1 + z_2)z_2/z_1$ which validates the applicability of Eq. S1 to our results even with an *incoherent source emanating from a large aperture*.

For $M \gg 1$, $F = \frac{z_1 + z_2}{z_1}$ approaches 1 such that Eq. S1 can be simplified as: $\Delta x_D \leq \frac{\lambda_0 z_2}{(L_C + L_H)}$. However, for $M \ll 1$, F approaches $1/M$ such that the pixel size requirement of Eq. S1 becomes much relaxed.

Therefore the analysis presented in Eq. S1 points to an important trade-off: To be able to use incoherent light through a large aperture (D) and still claim a decent spatial resolution based on lensfree holography, one would need a large M such that the smoothing effect of D/M on the cell image becomes negligible when compared to the target spatial resolution. However there is a price paid for this (described by Eq. S1), i.e., a smaller pixel size is now required when compared to $M \ll 1$ operating at a similar z_2 value. In conventional digital in-line holography systems, the pixel size requirement at the detector end is released approximately by a factor of F , which is referred to as the “*fringe magnification factor*” as also discussed in the previous section. With a large fringe magnification factor, the limiting effect of the pixel size on the extent of the hologram (L_H) is reduced, such that a much better resolution than the pixel size can be claimed. The down side of a large F is that the available field-of-view for a given detector array is also scaled down approximately by F^2 , reducing the overall field-of-view of the system. $M \gg 1$ choice implies a fringe magnification of unity ($F \approx 1$), which puts the burden on a tighter pixel size, while the requirements on the source spatial

coherence, mechanical stability, aperture size and cost are much relaxed together with a significant gain in the imaging field-of-view and light throughput. As highlighted in the Results and Discussion Sections, despite this tight pixel size requirement, a sub-pixel resolution can still be claimed in the presented lensless approach through iterative holographic reconstruction.

S2. Space-bandwidth product and lensfree cell holography

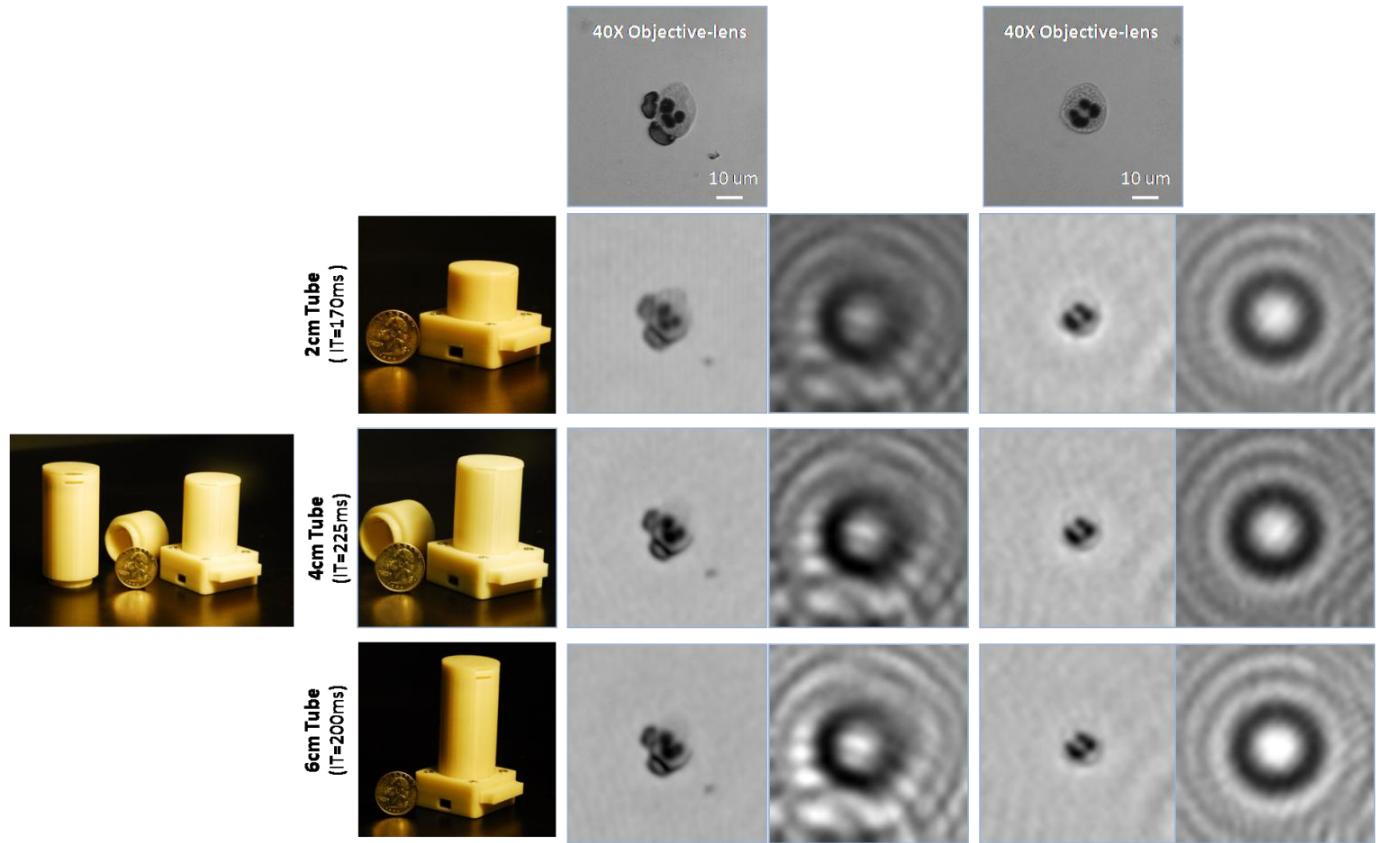
To better understand the space-bandwidth product requirements at the detector end for lensfree cell holography, let us denote the sensor width as W_D . Therefore, the space-bandwidth product (SB) of the detector can be written as $SB_D = \frac{W_D}{\Delta x_D}$. During coherent diffraction process, space-bandwidth product of a wave does not change; however, the space-frequency map (i.e., its Wigner distribution³⁷) gets distorted by a lateral shear without changing its area. This linear shear (which is proportional to $\lambda_0 \Delta z \Delta f$ in our case, where Δf is the spatial bandwidth of the cell's field transmission) also increases the required space-bandwidth product at the detector end. Therefore, in the presented incoherent holographic imaging approach, as a result of lensfree operation a space-bandwidth penalty of approximately $\lambda_0 \Delta z \Delta f^2$ is to be paid.³⁷⁻³⁸ Note that for $M \gg 1$ operation, according to Eqs. 3-4 of the Appendix, despite the incoherent source, each cell is coherently diffracting over an effective distance of Δz before being sampled by the detector. Therefore, the SB product that is required at the detector array to sample each cell hologram in our case can be approximated as $SB_C + \lambda_0 \Delta z \Delta f^2$ where $SB_C = L_C \cdot \Delta f$ is the original space-bandwidth product of the cell. As a result of this, the penalty of incoherent source and free space propagation is an increased SB product at the detector by $\lambda_0 \Delta z \Delta f^2$. Once again, a weakly scattering cell is assumed here where otherwise the intensity detection at the sensor array would have added an additional factor of 2 for the required space-bandwidth product since the self-interference terms will now start dominating the detected quantities.

This SB penalty gets smaller by choosing a small z_2 value, which is an argument in favor of $M \gg 1$. However, one should be careful with this statement: in the far-field region, where $M \gg 1$ is no longer valid, because of the spatial Fourier transformation through free space, the space-frequency map of a wave gets flipped by 90°, which implies that a space-bandwidth product of $L_C \cdot \Delta f$ would be sufficient for the detector end, which this time detects the Fourier transform intensities. Another way

of stating this conclusion is that Fresnel diffraction requires a significant penalty for space-bandwidth product at the detector end, whereas the Fourier transform plane (i.e., Fraunhofer region) is still as efficient as the original image in terms of the space-bandwidth product requirement for detection. Thus, *the price that is paid for a lensless system is an increased space-bandwidth product when compared to Fourier or image plane (i.e., lens-) based detection*. In the case of $M \ll 1$, of course, the imaging field-of-view will be significantly reduced when compared to $M \gg 1$ case, as well as the individual holographic signatures of the cells will be lost, which can be considered as a loss for diagnostic purposes as the 2D texture of holographic cell signatures is also valuable for cytometry applications.²²

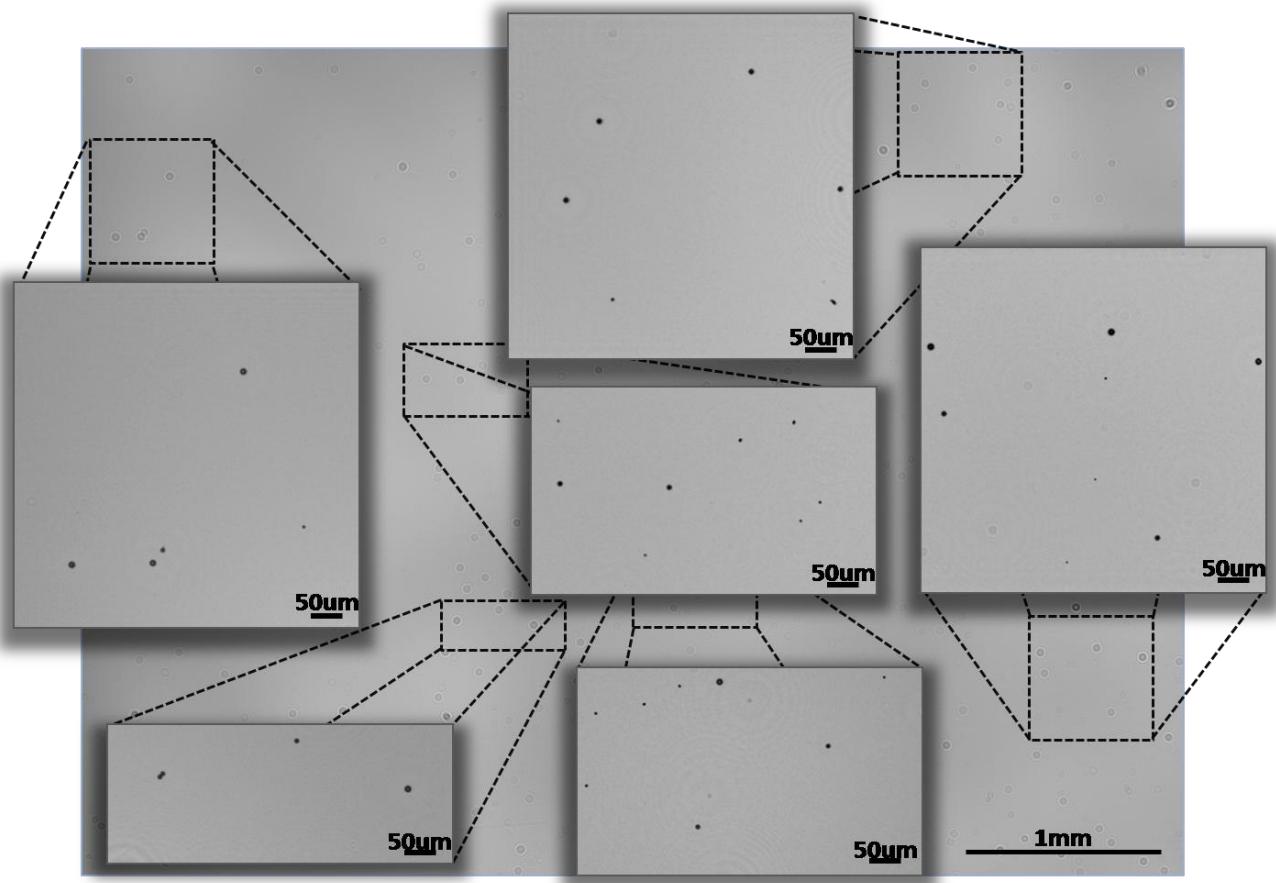
SUPPLEMENTARY FIGURES

SUPPLEMENTARY FIGURE 1



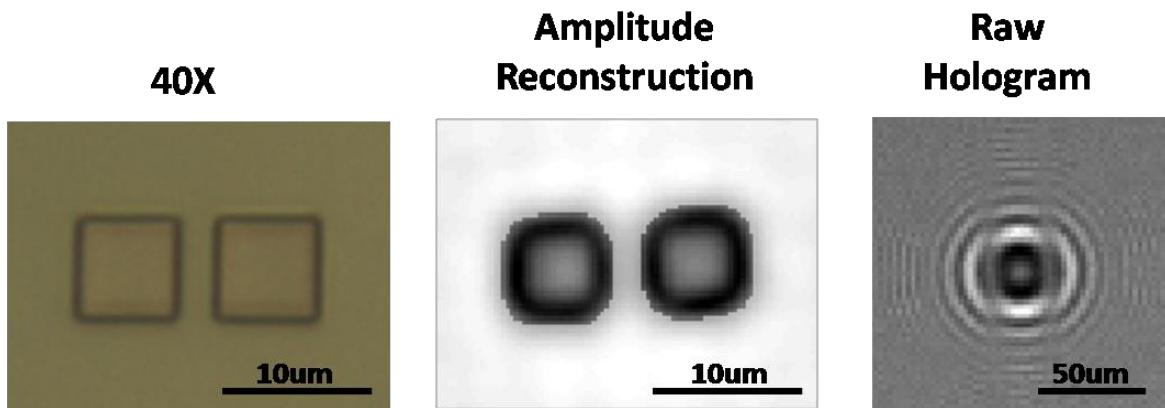
Supplementary Figure 1. Same as Fig. 3 of the main text, except for different tube designs. In the main text, Fig. 3 illustrates the performance of the 4 cm tube design (shown in Fig. 1(a)), whereas here we compare the imaging performances of 2, 4 and 6 cm tubes against a 40X objective-lens (NA=0.6). IT: integration time of the acquired raw lensfree hologram, shown to the right of each reconstructed image.

SUPPLEMENTARY FIGURE 2



Supplementary Figure 2. Full field-of-view reconstructed image of a sample that is composed of 3, 7 and 10 μm polystyrene particles is illustrated. The raw holographic image is captured using the lensfree microscope of Fig. 1(a).

SUPPLEMENTARY FIGURE 3



Supplementary Figure 3. A test feature is imaged using the lensless holographic microscope with an LED at 591nm ($D=50\ \mu\text{m}$, $z_1=\sim 3\text{cm}$ and $z_2=\sim 0.7\text{mm}$) and is compared against a 40X objective-lens (NA=0.6) image. The gap between the squares is estimated as $1.94\ \mu\text{m}$ (FWHM) from the reconstructed image, which matches very well with the gap estimate from the 40X image ($1.95\ \mu\text{m}$ FWHM). Integration time for the raw hologram: <150 ms.