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29 September 2021

Computational Light-Field Microscopy and an Application in Neuroscience

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Joint work with

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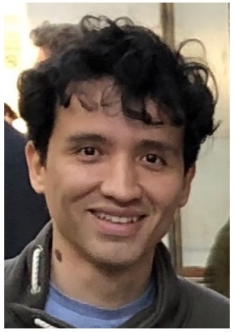

Amanda Foust

Imperial College London

Outline

- Multi-photon microscopy and neuroscience
- The image formation process in light-field microscopy (LFM)
- Volume reconstruction
  - Discretization of the forward model
  - Reconstruction based on ADMM

  On going work: extension of the model-based approaches to deep learning via unfolding
- Localization of neurons using LFM
  - EPI structure and EPI dictionary
  - Localization based on convolutional sparse coding

  On going work: extension of the model-based approaches to deep learning via unfolding
- Conclusions

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Two-Photon Microscopy for Neuroscience

- Goal of Neuroscience: to study how information is processed in the brain
- Neurons communicate through pulses called Action Potentials (AP)
- Need to measure in-vivo the activity of large populations of neurons at cellular level resolution
- Two-photon microscopy combined with right indicators is the most promising technology to achieve that

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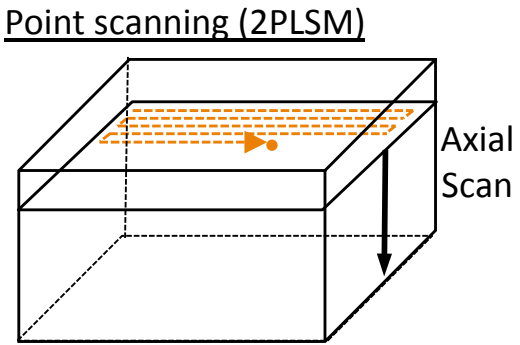
Two-Photon Microscopy

- Fluorescent sensors within tissues
- Highly localized laser excites fluorescence from sensors
- Photons emitted from tissue are collected
- Focal spot sequentially scanned across samples to form image



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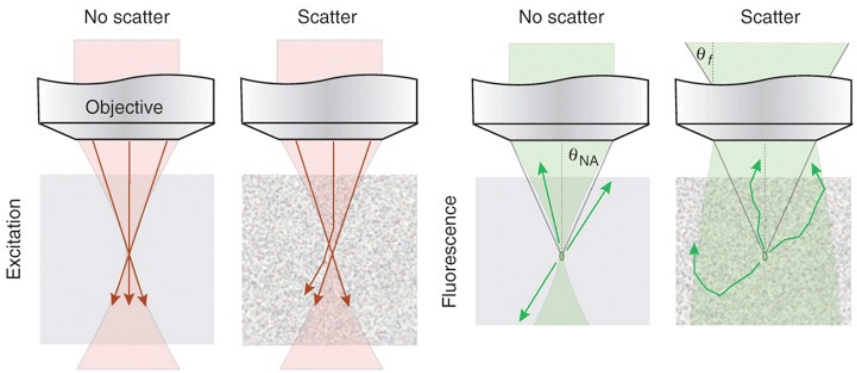
Two-Photon Microscopy

- Fluorescent sensors within tissues
- Highly localized laser excites fluorescence from sensors
- Photons emitted from tissue are collected
- Focal spot sequentially scanned across samples to form image
- Two-photon microscopes in raster scan modality can go deep in the tissue but are slow



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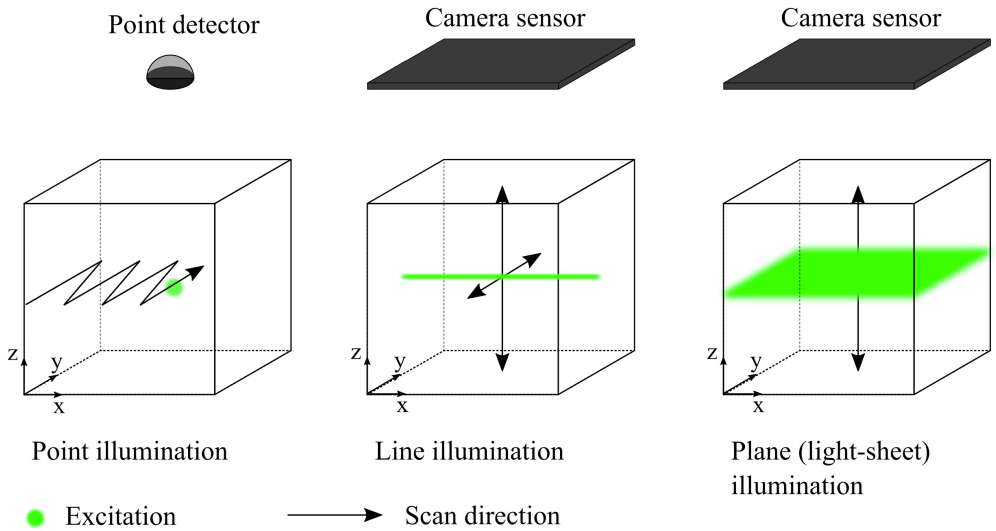
Two-Photon Microscopy

- In order to speed up acquisition one can change the illumination strategy
- This mitigates the issue but does not fix it



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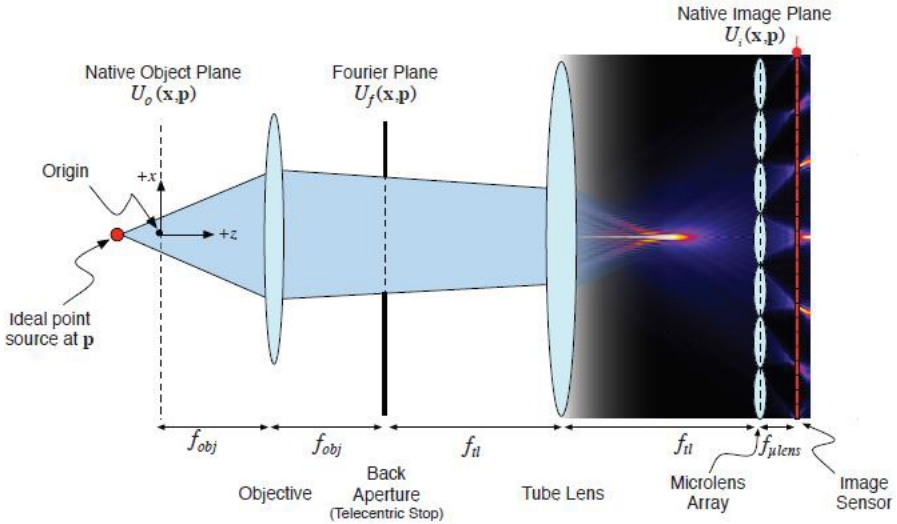
Light-field Microscopy

Light-Field Microscopy (LFM) is a high-speed (scan-less) imaging technique that uses a simple modification of a standard microscope to capture a 3D image of an entire volume in a single camera snapshot



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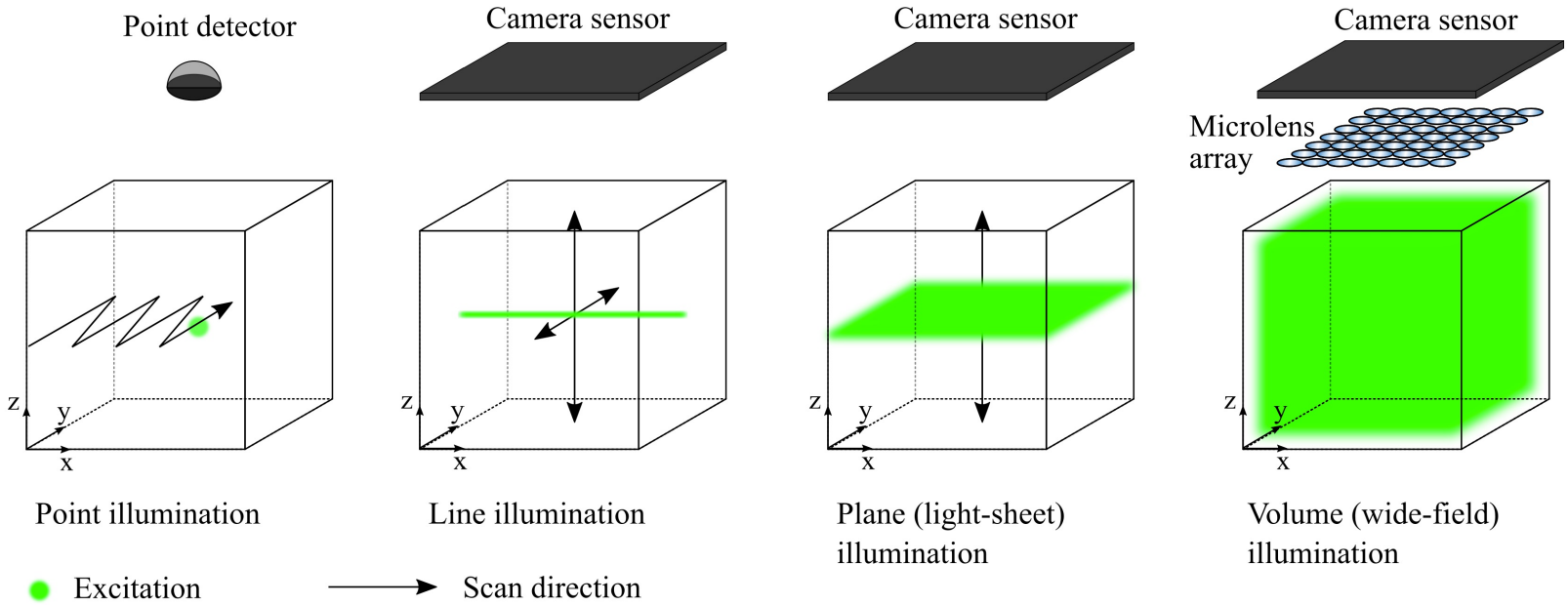
Light-field Microscopy and Illumination Strategies



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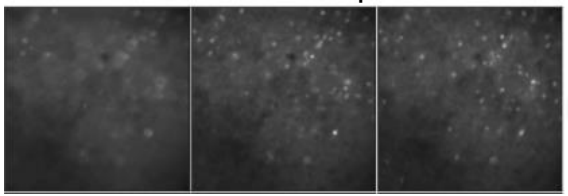
Light-field Microscopy

2048x2048x41 pixels



z=-8μm z=0μm z=8μm

Input Volume

Brain slice (50 μm thick) taken from a GFP Tagged triple transgenic mouse line using our light field microscope

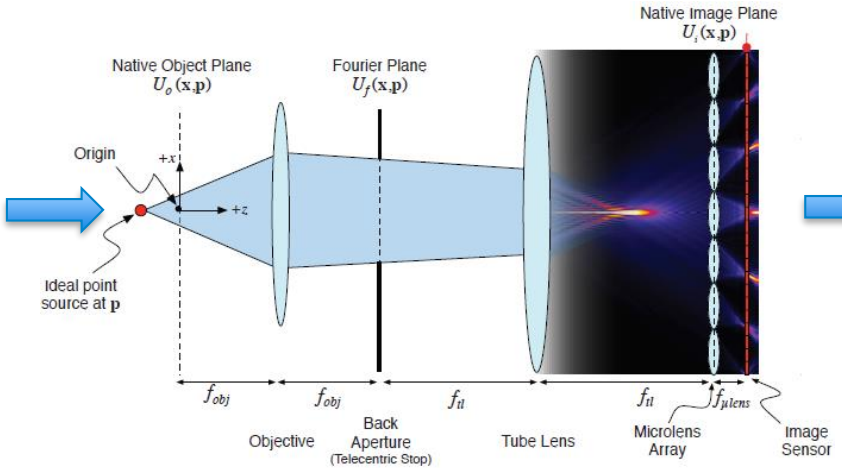
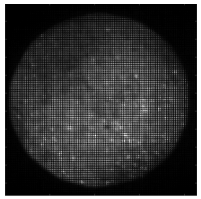


Image taken from [2]

2048x2048 pixels



Measured LF

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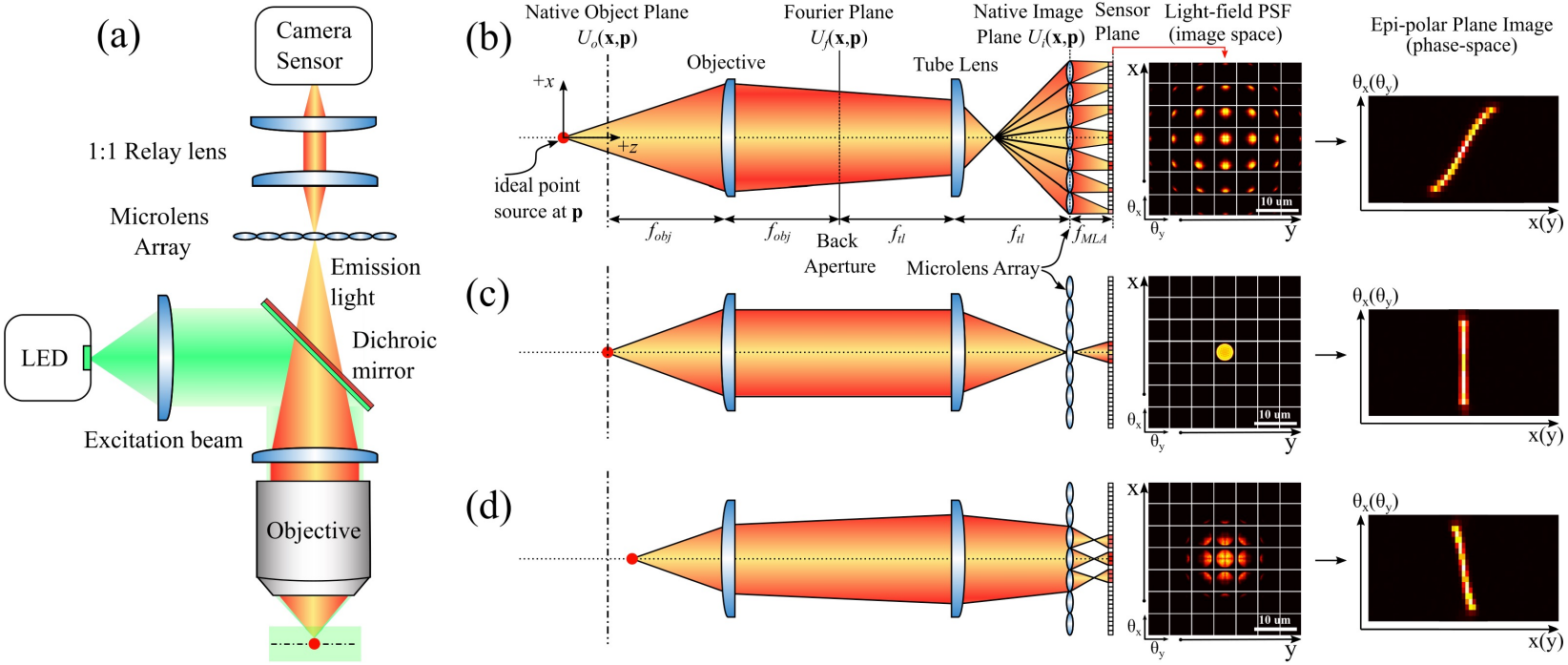
Light-field Microscopy



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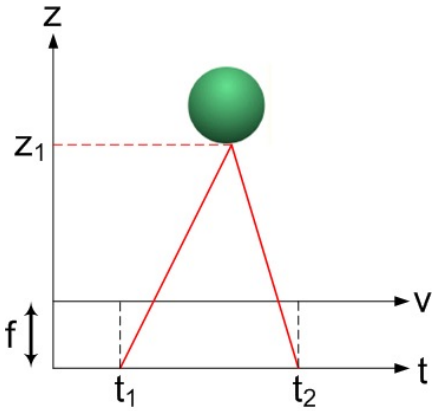
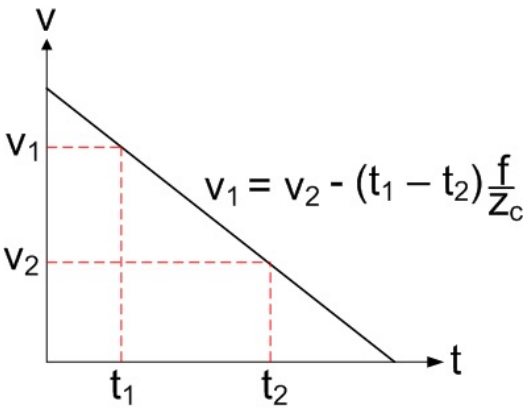
Epipolar Plane Image (EPI)

- Taking one slice of the lightfield leads to the EPI
- Points are mapped onto lines in the (EPI)
- Slope of lines are inversely proportional to the depth
- Lines with larger slopes occlude lines with smaller slopes





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IBR Results on the Lightfield

Pearson et al. IEEE TIP 2013

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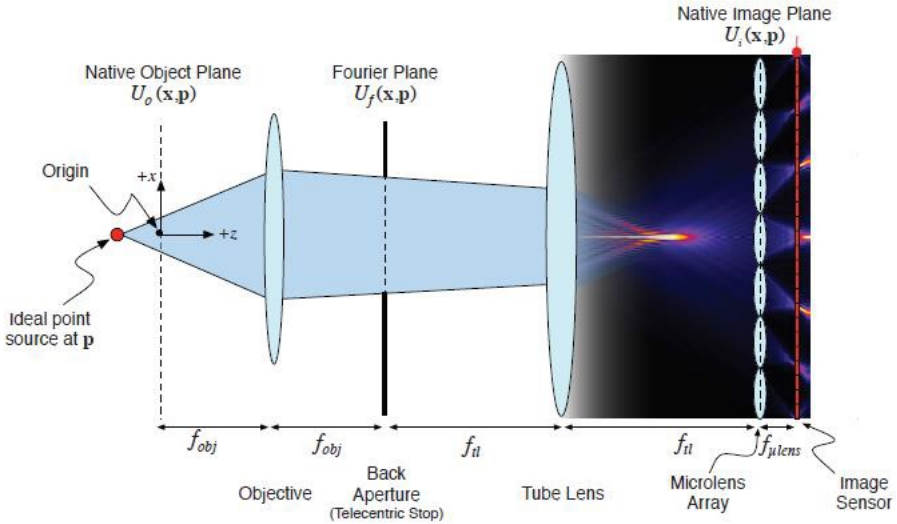
Light-field Microscopy

- Challenges
  - Cannot use ray approximation (geometric optics) to model the image formation. Need to use wave optics
  - Scattering induces blur, making inversion more challenging

- Opportunities
  - Data is sparse (neurons fire rarely and are localized in space)
  - Occlusion can be ignored
  - Localization of neurons is often sufficient (no need for high-quality volume reconstruction)



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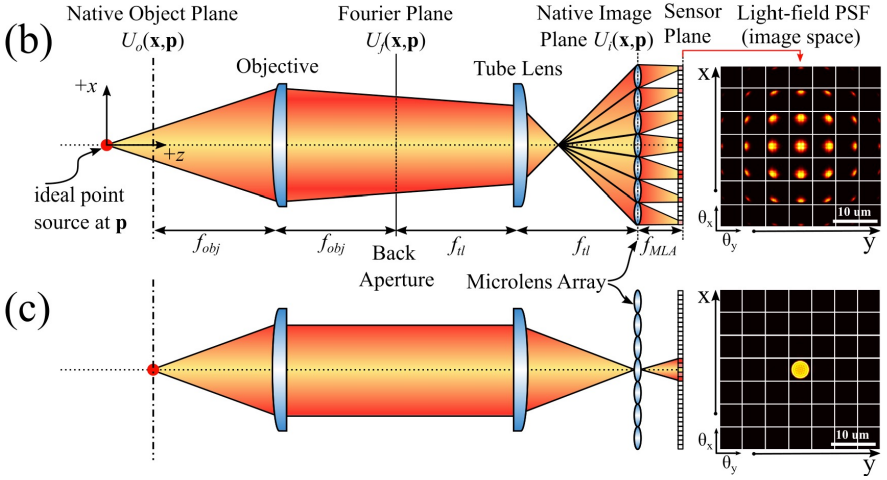
Light-field Microscopy – Wave Model

- Wave Optics model [Broxton et al. 2013]
- Based on estimating the wavefront at three specific points:
  - Use Debye theory to compute the wavefront at NIP
  - Microlens array (MLA) then makes the PSF periodically shift invariant
  - Use Fresnel diffraction solution to estimate the wavefront at the sensor plane



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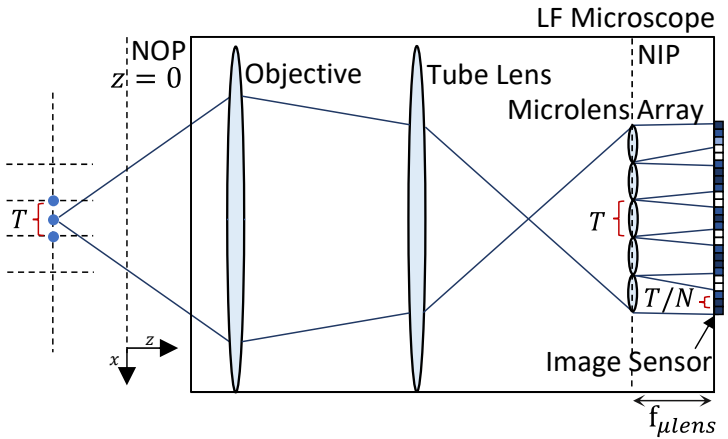

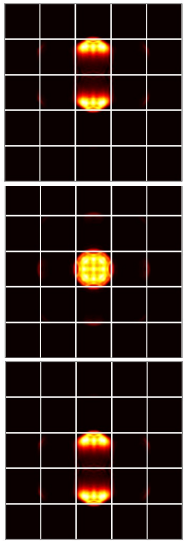

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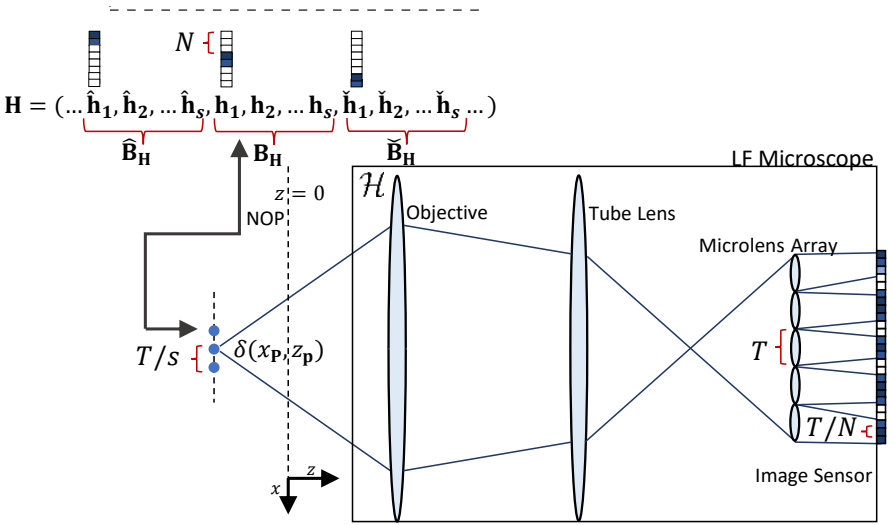
Discretization of the Forward Model

- Given the expression of the wavefront per point source
- The PSF $h(\boldsymbol{p}, \boldsymbol{x})$ is discretized by shifting the point source along a grid and by storing the sampled light-field pattern. This leads to the discrete system $\boldsymbol{g} = \boldsymbol{H}\boldsymbol{f}$
- Issue:
  - the signal might be better modelled using an elementary function different from a Dirac
  - Dependency across depths not exploited
  - Blocking artefacts at the native object plane



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Volume Reconstruction from LF Data

- Given $\boldsymbol{g} = \boldsymbol{H}\boldsymbol{f}$ reconstruction of $\boldsymbol{f}$ can be problematic
  - $\boldsymbol{H}$ is ill-conditioned
  - Note that $\boldsymbol{H}$ is block-circulant (periodically shift invariant) and can be modelled with a filter-bank

- Approach:
  - Use generalized sampling theory to improve the discretization
  - Use SVD to simplify the forward model
  - Inversion based on stronger priors and ADMM

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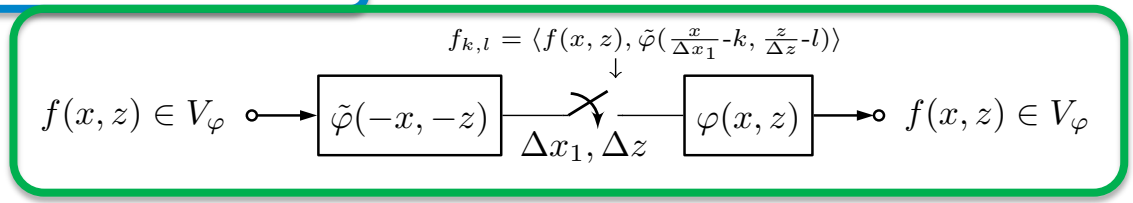
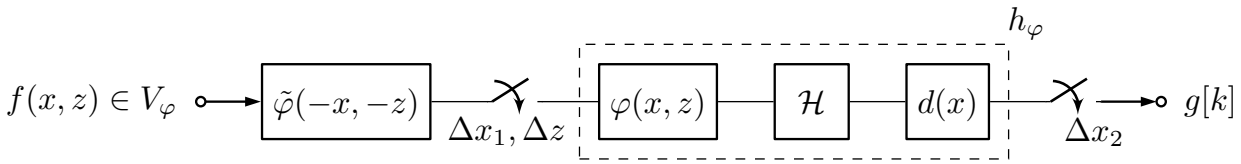
Discretization of Forward Model

- New discretization
  - $f(x,z)$ is assumed to belong to a shift-invariant space generated by $\varphi(x,z)$:

$f(x,z) = \sum_{k,l} f_{k,l}\varphi(x-k, z-l)$ where $f_{k,l} = \langle f(x,z), \tilde{\varphi}(x-k, z-l)\rangle$



- We use linear splines as $\varphi(x,z)$. This leads to a new better-conditioned $\boldsymbol{H}$



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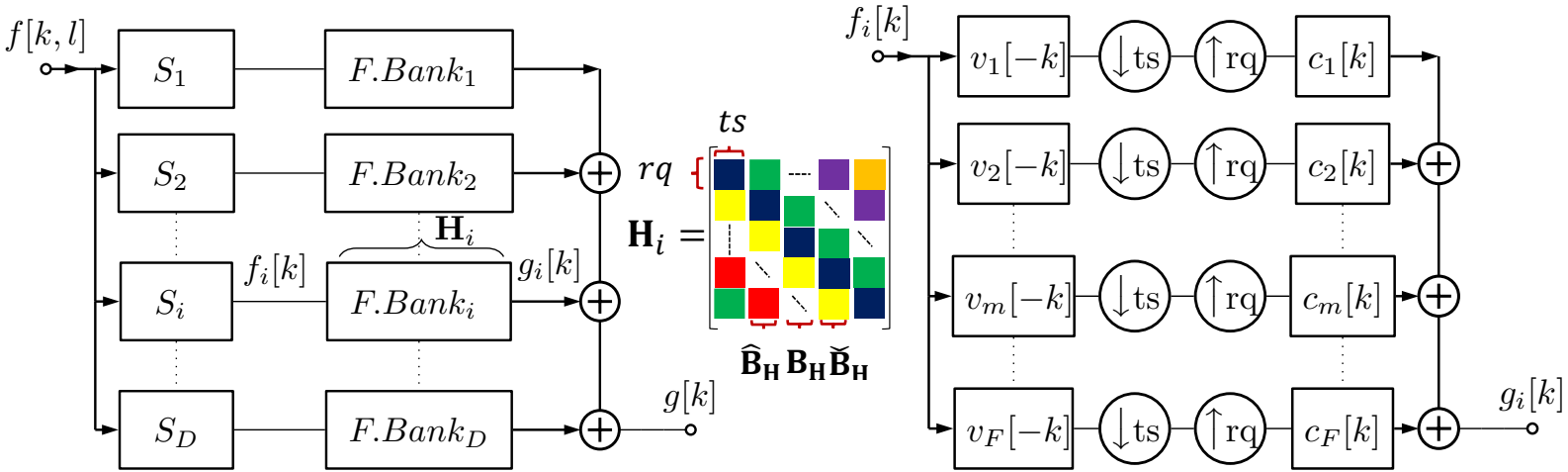
Discretization of Forward Model

- The forward model is periodically shift invariant and so can be modelled wit a filter-bank



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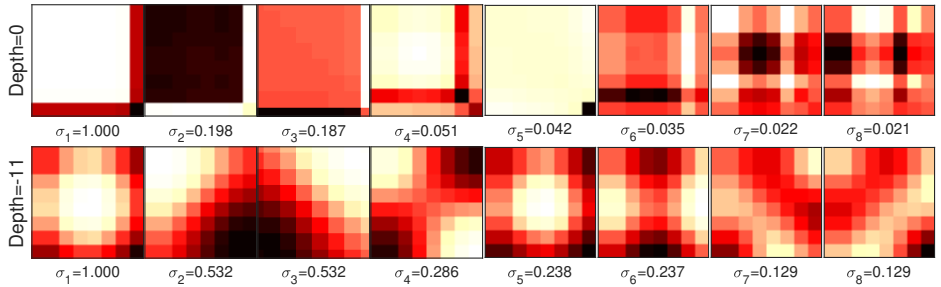
Discretization of Forward Model

- The new filters related to $\boldsymbol{H}$ are more stable:

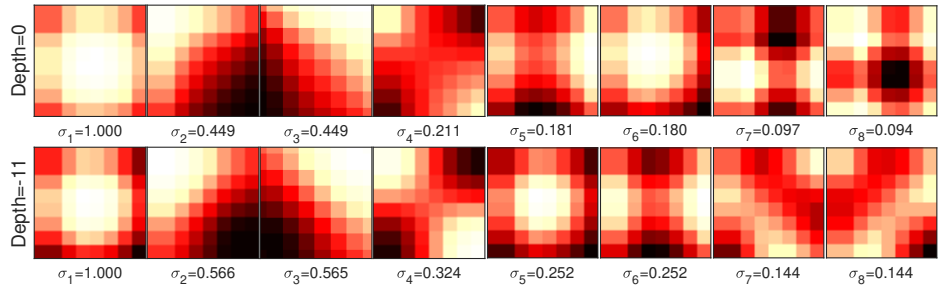
Old discretization

a)



New discretization

b)



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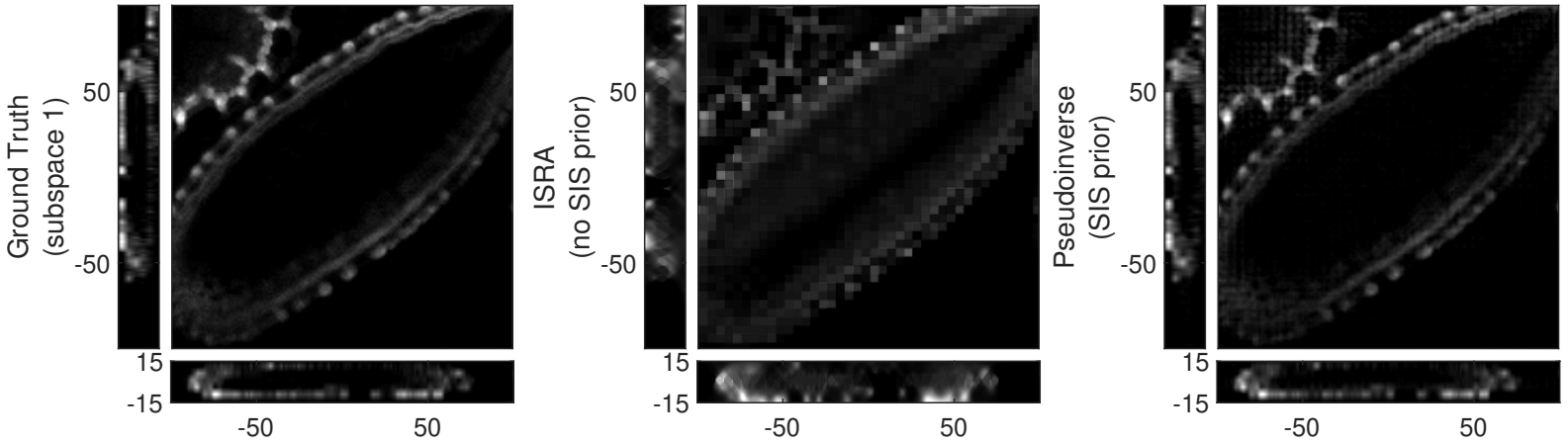
Volume Reconstruction from LF Data

- “Linear” reconstruction with the new forward model does not suffer from blocking artefacts:

$$\boldsymbol{g = Hf}$$



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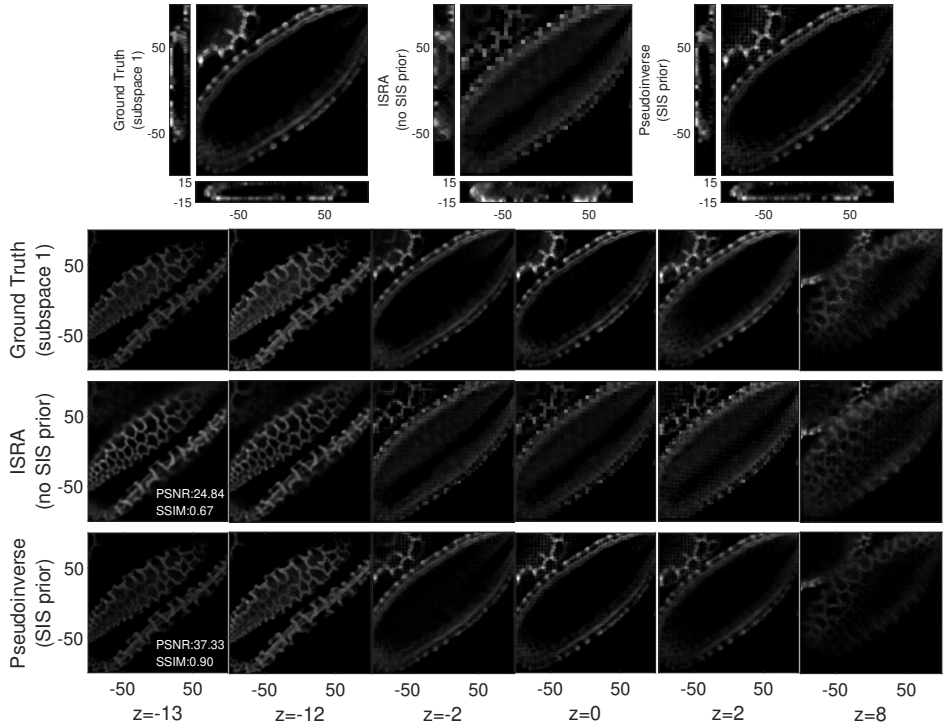

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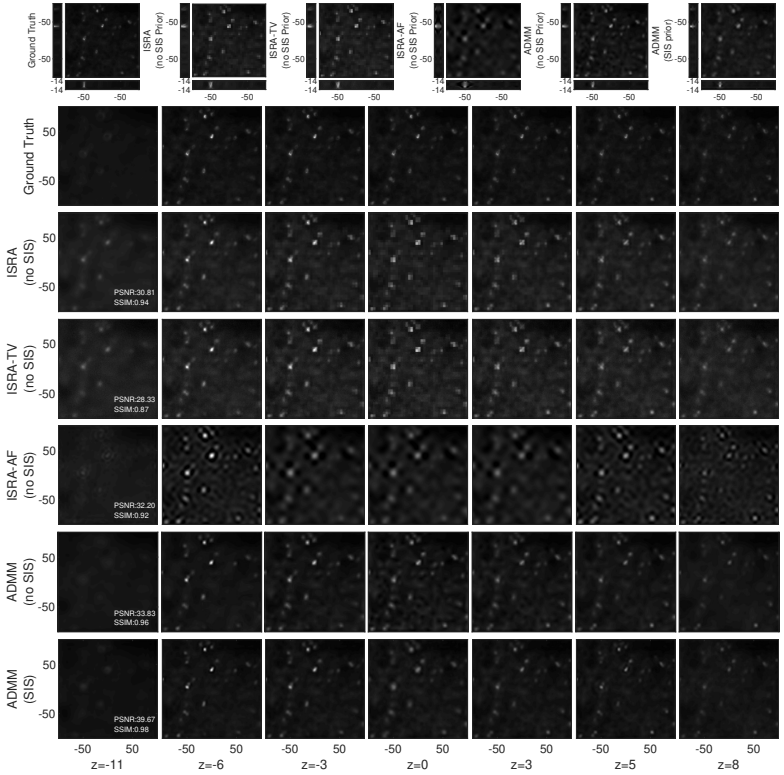
Volume Reconstruction from LF Data

- Further improvements are possible by adding further priors:

$$\min_{\mathbf{f}} \quad \|\mathbf{H}_\delta \mathbf{S}_\varphi \mathbf{A}_\varphi \mathbf{f} - \mathbf{g}\|_2^2 + \|\mathbf{D}_x^n \mathbf{f}\|_1 + \|\mathbf{D}_y^n \mathbf{f}\|_1 + \|\mathbf{D}_z^n \mathbf{f}\|_1$$
$$\text{s.t.} \quad \mathbf{f} \geq \mathbf{0},$$

- Optimization solved using ADMM



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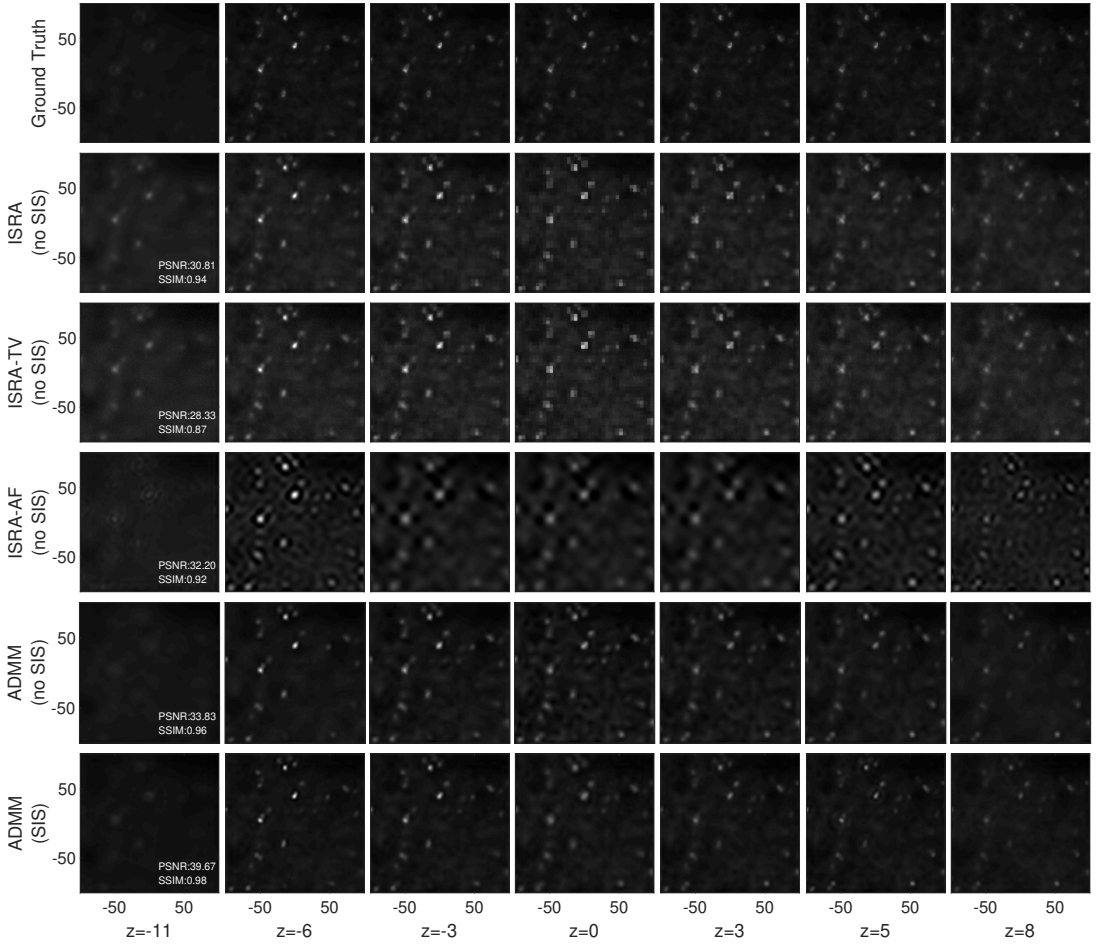

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Volume Reconstruction from LF Data

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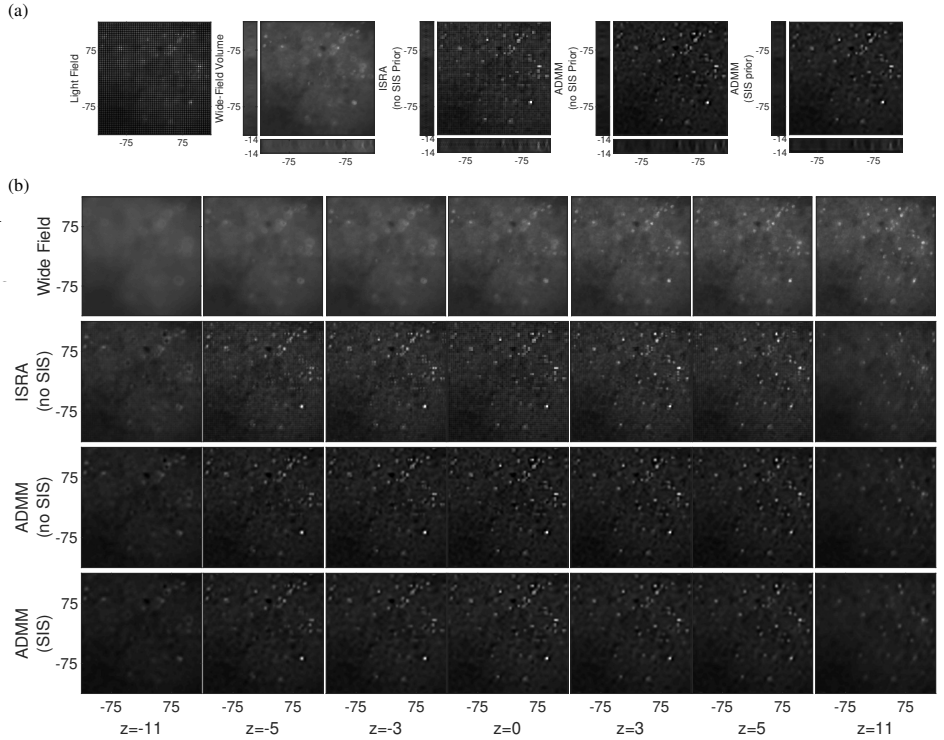

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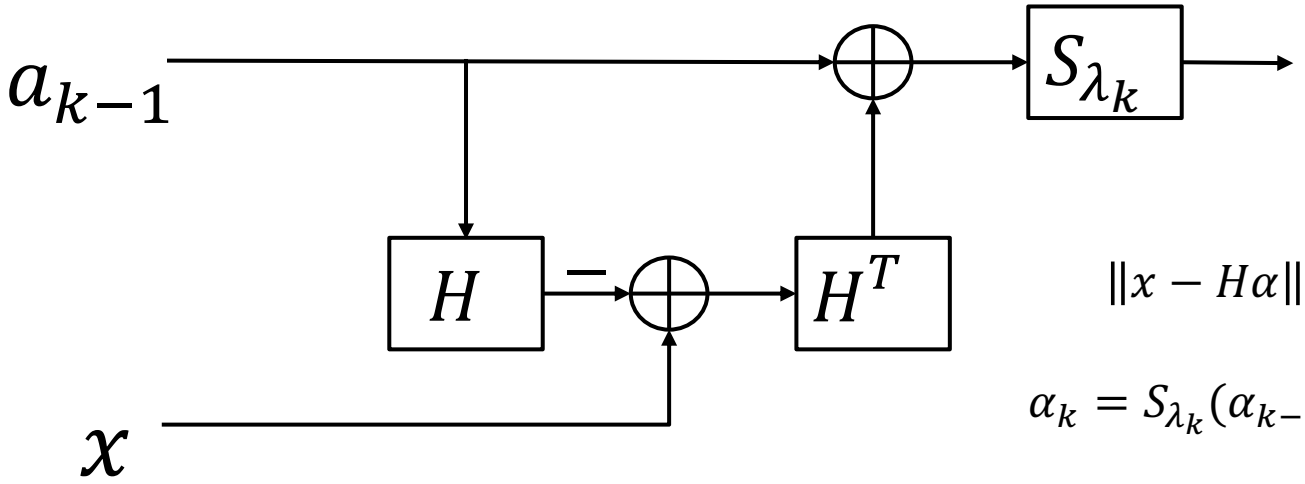
On-going: Learning-based Reconstruction



$$\|x - H\alpha\|^2 + \lambda\|\alpha\|_1$$

$$\alpha_k = S_{\lambda_k}(\alpha_{k-1} + H^T(x - H\alpha_{k-1}))$$

Inspired by LISTA[1], we “unfold” this iteration to obtain a deep network

[1]Gregor Karol and LeCunYann, “Learning fast approximations of sparse coding ”, Proceedings of the 27th International Conference on International Conference on Machine Learning, 2010

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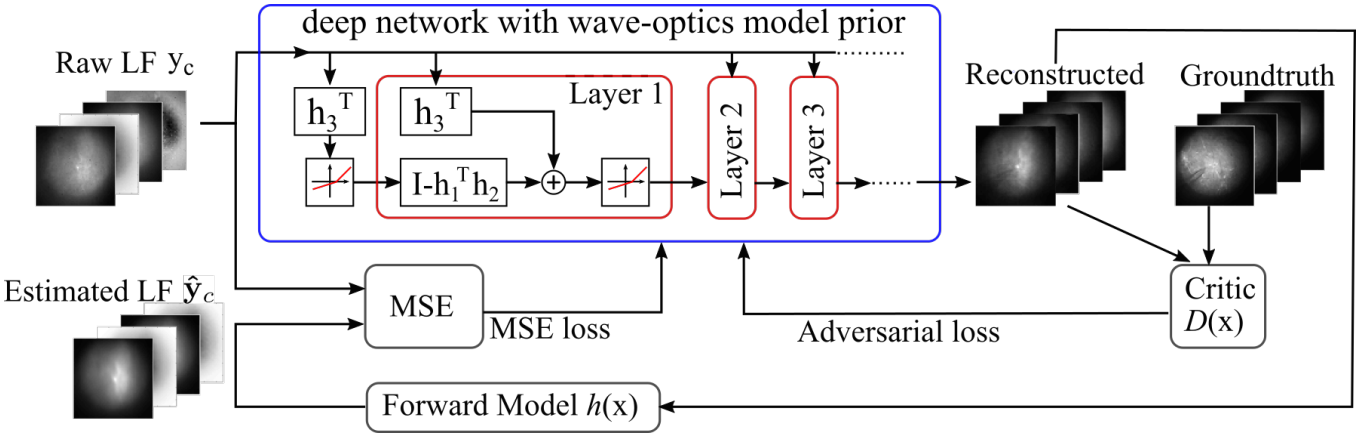
On-going: Learning-based Reconstruction

- Combines the light-field wave-optics model with Learned Iterative Shrinkage-Thresholding Algorithm (LISTA)
- Un-paired data calls for adversarial network



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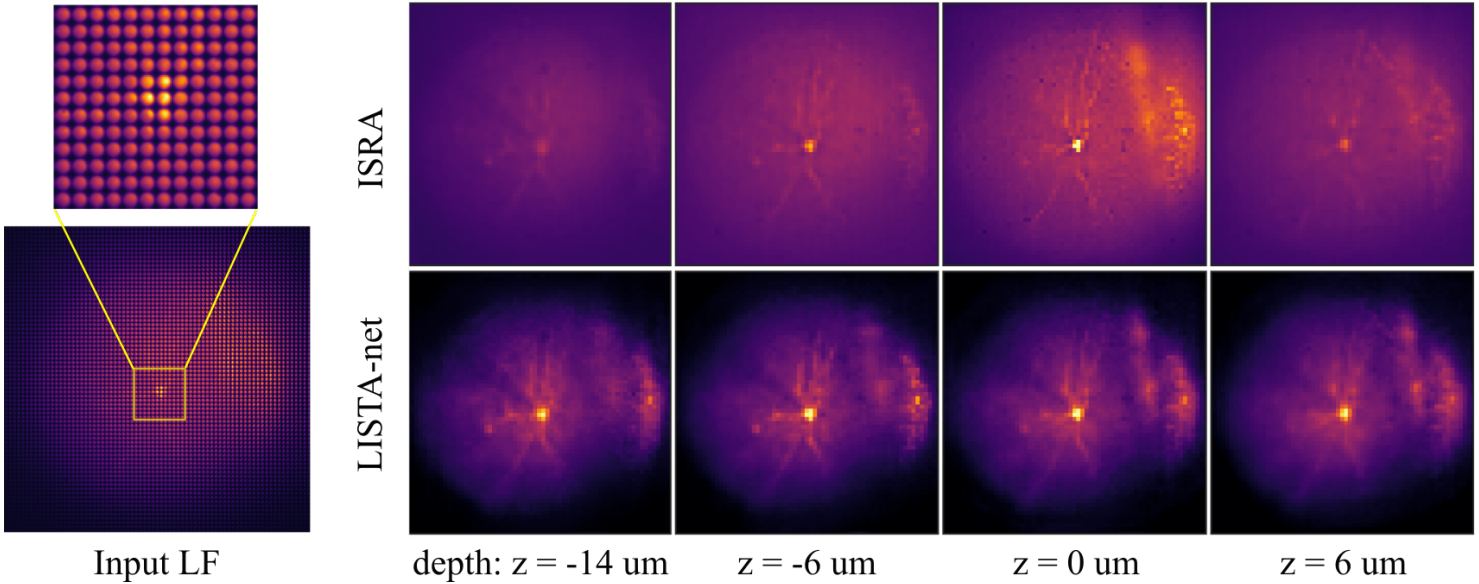
Learning-based Reconstruction- Results



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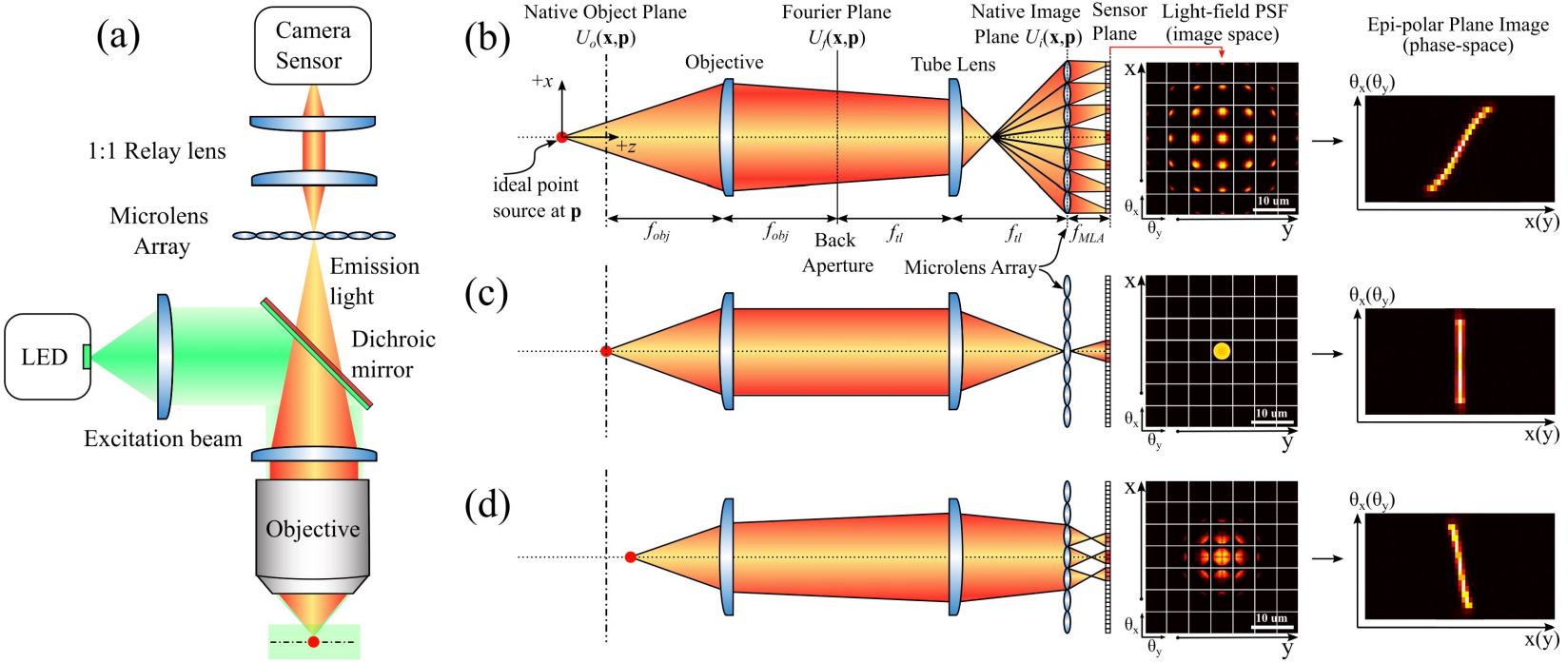
Localization of Neurons using LFM



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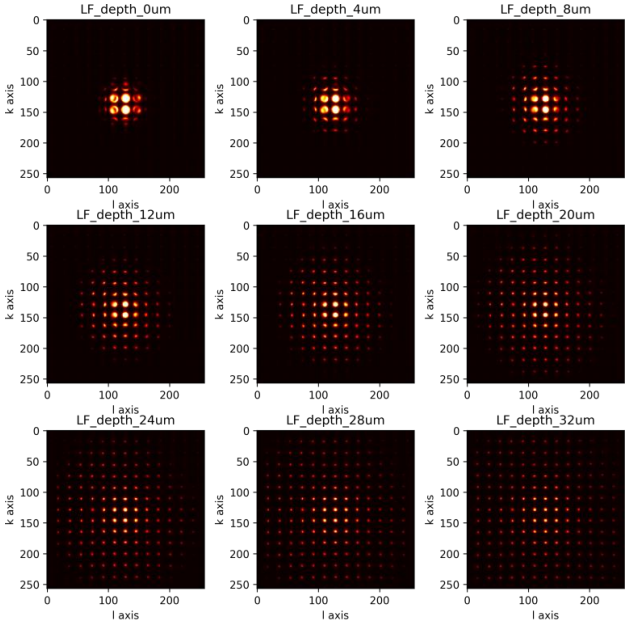
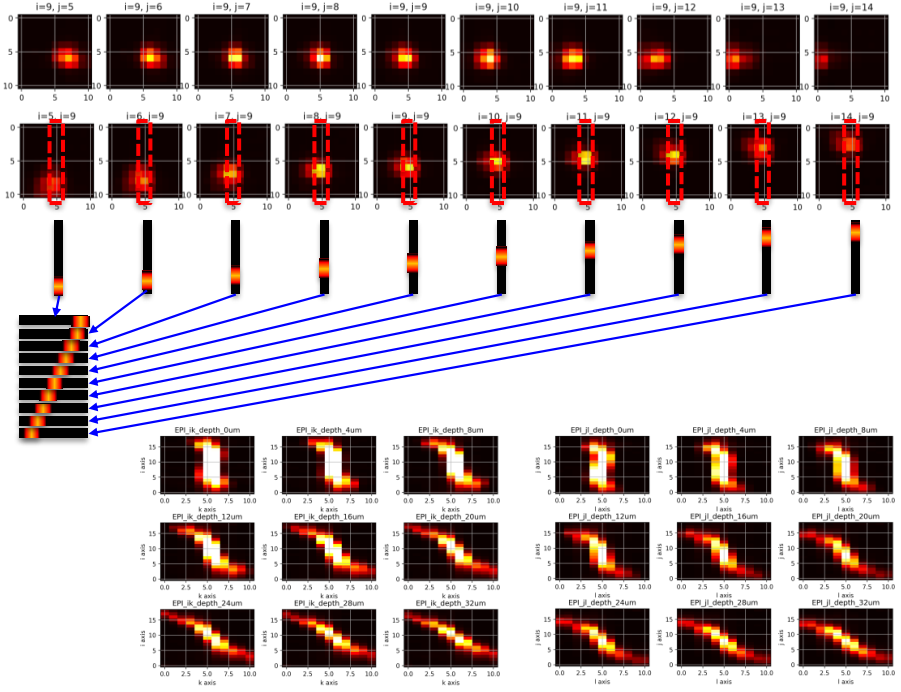
Real Lightfield Images and EPIs



Real LFM for a bead in different depths ranging from 0 to 32 um

Sub-aperture images along vertical and horizontal directions



EPIs from real LFM data. i-k direction (left) and j-l direction (right)

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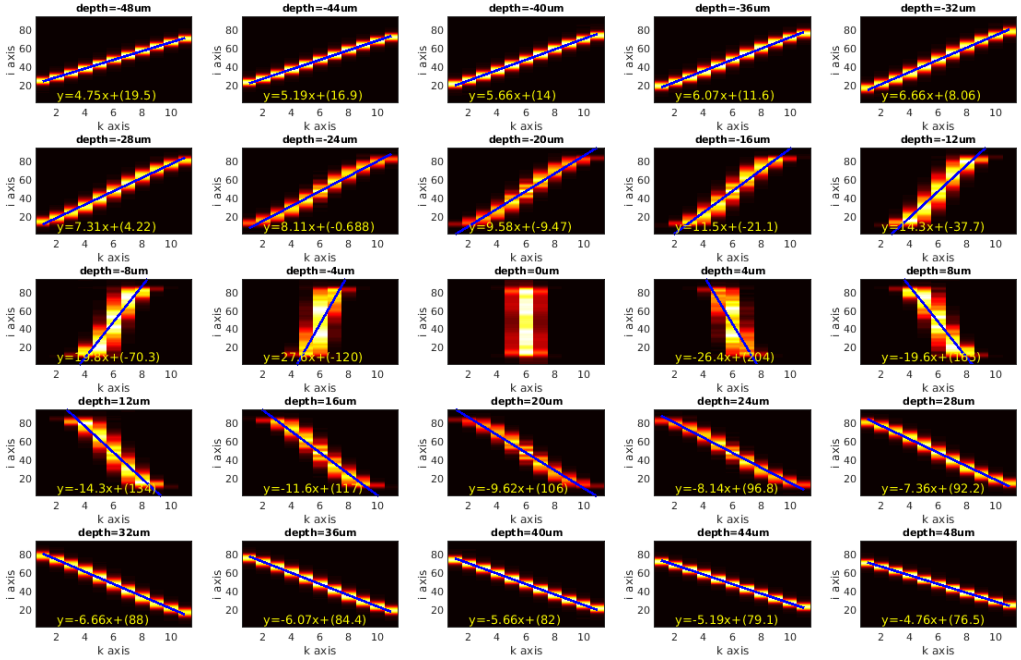
Dictionary of EPI from Simulated Lightfield Microscope



Simulated EPI dictionary. Each atom corresponds to a specific depth

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Convolutional Sparse Coding via ADMM

We develop a convolutional sparse coding algorithm to decompose the input EPI into latent factors to estimate depth and spatial locations.

Objective in image domain:

$$\min_{\mathbf{z}} \quad \frac{1}{2}\|\mathbf{Y} - \sum_{m=1}^{M} \mathbf{d}_m * \mathbf{z}_m\|_2^2 + \beta \sum_{m=1}^{M} \|\mathbf{z}_m\|_1$$

Objective in Fourier domain:

$$\min_{\mathbf{z}_m} \quad \frac{1}{2}\|\hat{\mathbf{Y}} - \sum_{m=1}^{M} \hat{\mathbf{d}}_m \odot \hat{\mathbf{z}}_m\}\|_2^2 + \beta \sum_{m=1}^{M} \|\mathbf{z}_m\|_1$$

Objective in matrix format:

$$\min_{\mathbf{Z}} \quad \frac{1}{2}\|\hat{\mathbf{Y}} - \hat{\mathbf{D}}\hat{\mathbf{Z}}\|_2^2 + \beta \|\mathbf{Z}\|_1$$

Lagrangian

$$\mathcal{L}(\mathbf{Z}, \mathbf{T}, \boldsymbol{\gamma}) = \frac{1}{2}\|\mathbf{Y} - \mathbf{D}\mathbf{Z}\|_2^2 + \beta\|\mathbf{T}\|_1 + \boldsymbol{\gamma}^\top(\mathbf{Z} - \mathbf{T}) + \frac{\mu}{2}\|\mathbf{Z} - \mathbf{T}\|_2^2$$

ADMM algorithm for solving CSC

$$\mathbf{Z}^{(i+1)} = \arg\min_{\mathbf{Z}} \mathcal{L}(\mathbf{Z}, \mathbf{T}^{(i)}, \boldsymbol{\gamma}^{(i)})$$
$$= \mathcal{F}^{-1}\{(\hat{\mathbf{D}}^\top\hat{\mathbf{D}} + \mu\mathbf{I})^{-1}(\hat{\mathbf{D}}^\top\hat{\mathbf{Y}} - \hat{\boldsymbol{\gamma}} + \mu\hat{\mathbf{T}}^{(i)})\}$$

$$\mathbf{T}^{(i+1)} = \arg\min_{\mathbf{T}} \mathcal{L}(\mathbf{Z}^{(i+1)}, \mathbf{T}, \boldsymbol{\gamma}^{(i)})$$
$$= \mathbf{S}_{\beta/\mu}(\mathbf{Z}^{(i+1)} + \boldsymbol{\gamma}^{(i)}/\mu)$$

$$\boldsymbol{\gamma}^{(i+1)} = \arg\min_{\boldsymbol{\gamma}} \mathcal{L}(\mathbf{Z}^{(i+1)}, \mathbf{T}^{(i+1)}, \boldsymbol{\gamma})$$
$$= \boldsymbol{\gamma}^{(i)} + \mu(\mathbf{Z}^{(i+1)} - \mathbf{T}^{(i+1)})$$

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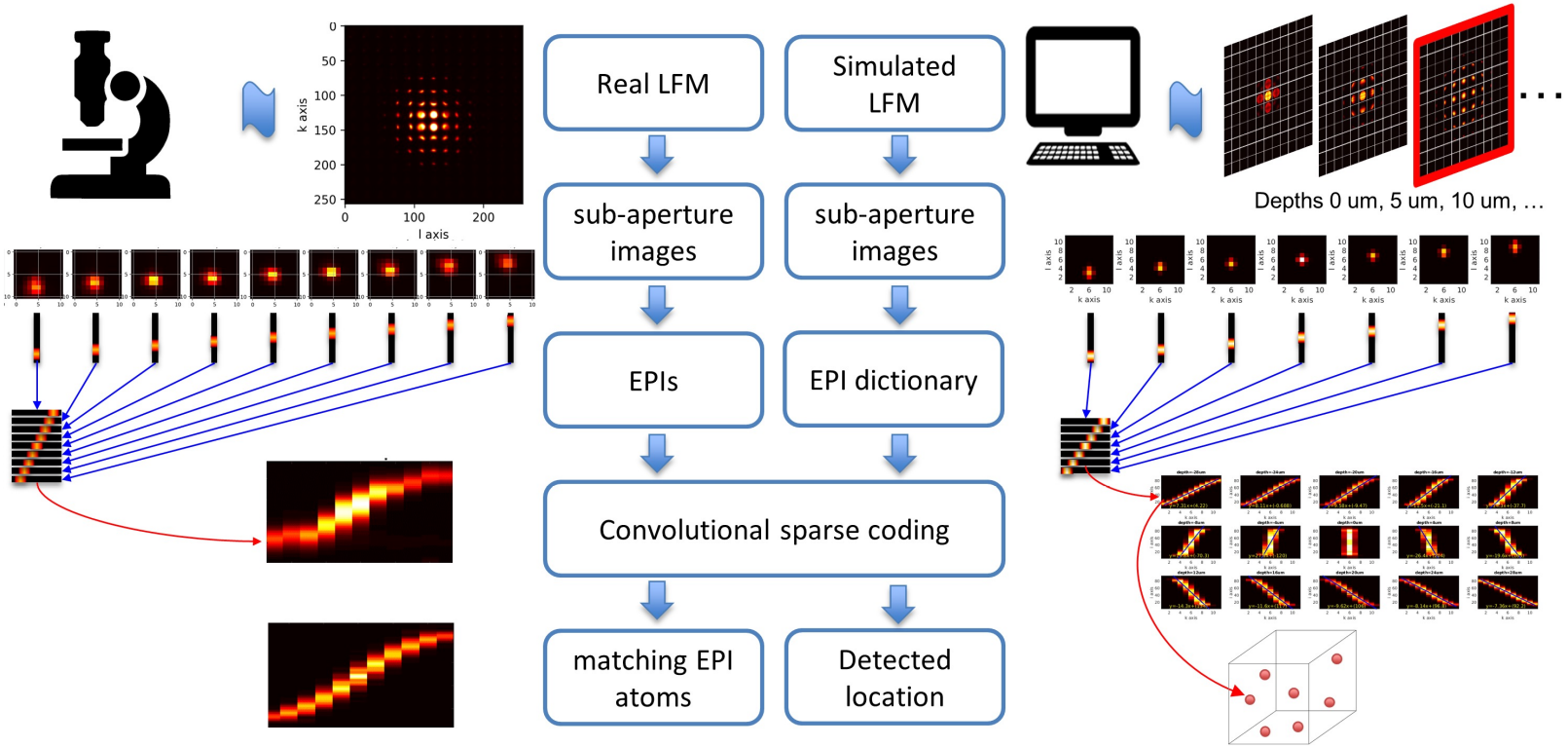
Neuron Localization Approach



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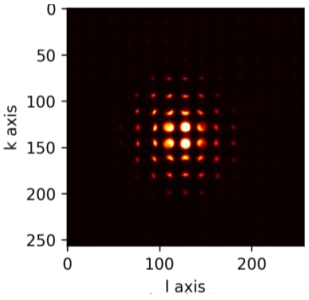
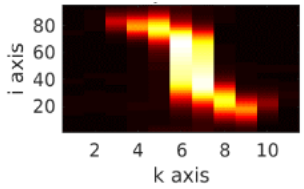
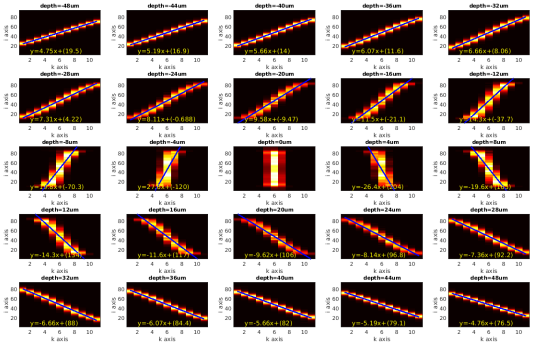
Location Estimation Algorithm



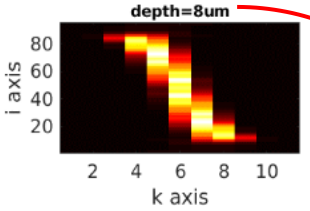
Input EPI



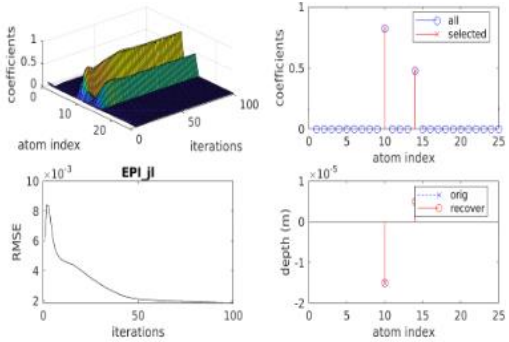


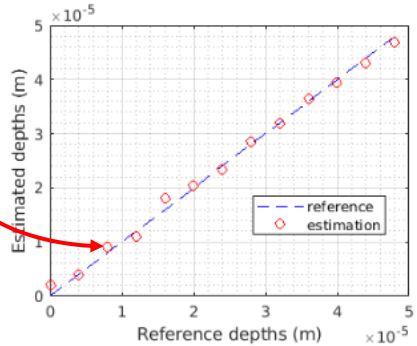
Simulated EPI dictioary

Convolutional sparse coding



Reconstructed EPIs





Depth estimation

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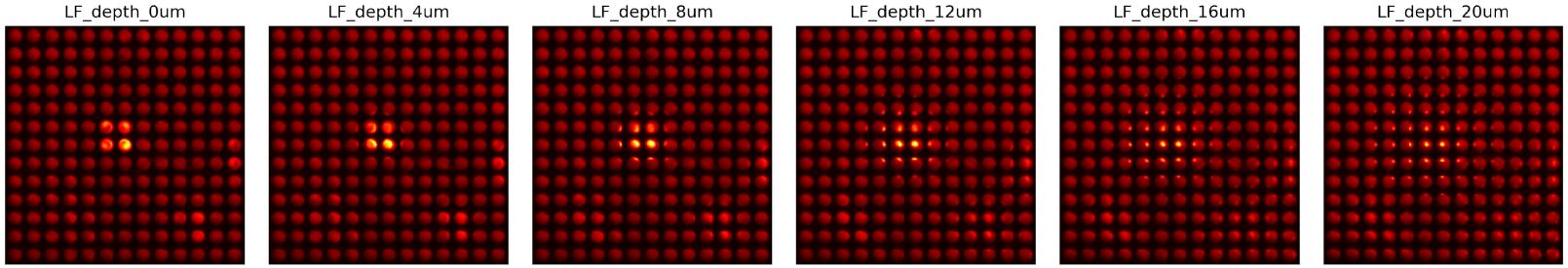
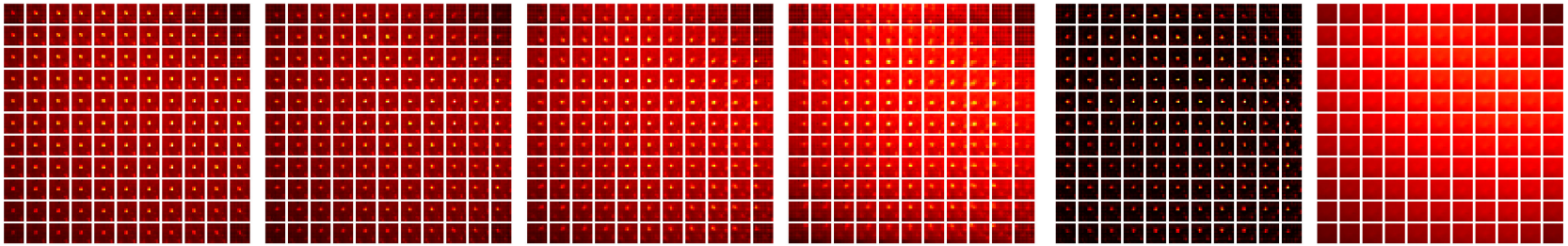
Numerical Results



(a) Raw LFM data for a neuronal cell at different depths away from the focal plane.



(b) Sub-aperture image arrays for depth 0, 12, 24 and 36 μm, respectively.

(c) Foreground and Background at depth 12 μm

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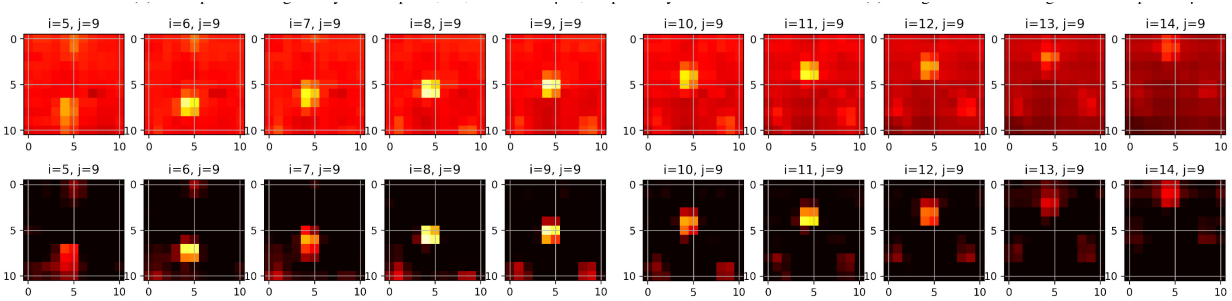
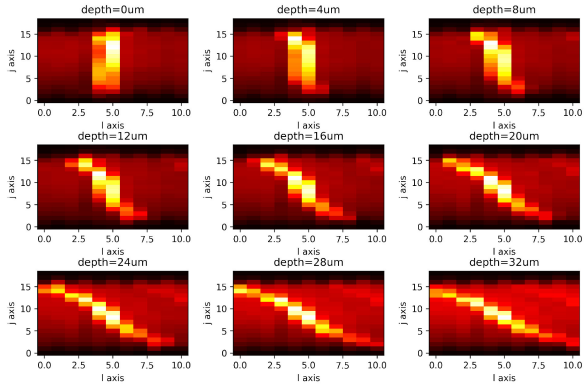
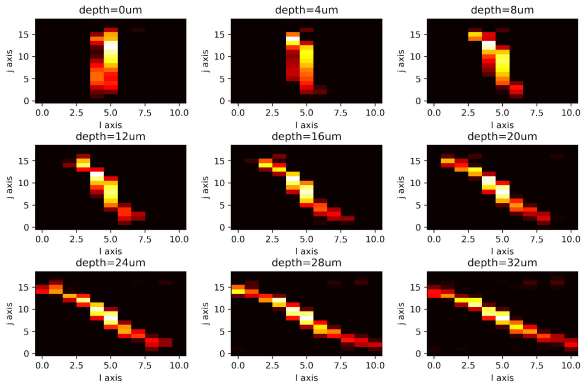
Numerical Results



(d) The central column of the sub-aperture image array at depth 36 μm. View changes from down to up. Above: with background. Below: background is removed.



(e) Constructed EPIs in the $j-l$ space.



Purified EPIs in the $j-l$ space without background.

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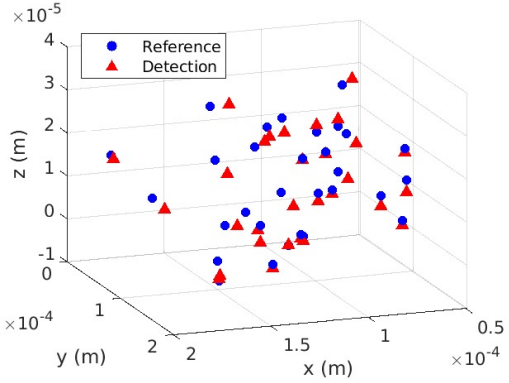
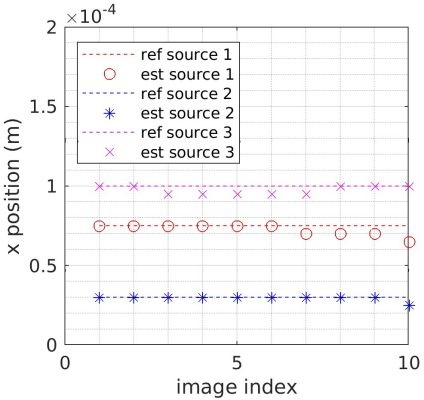
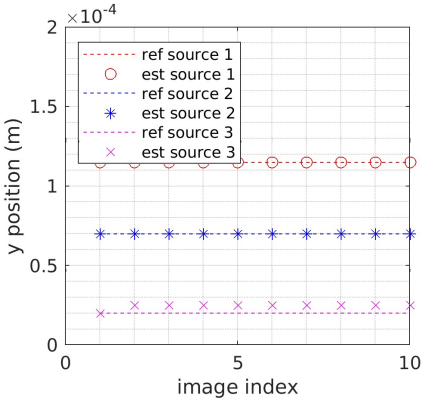
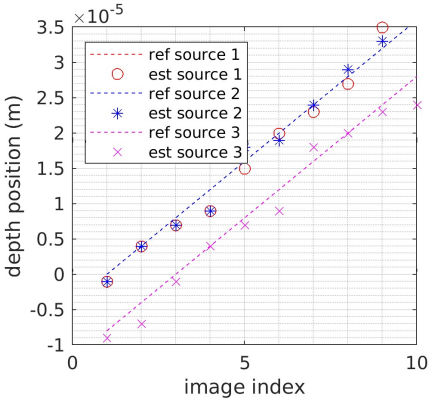
Numerical Results









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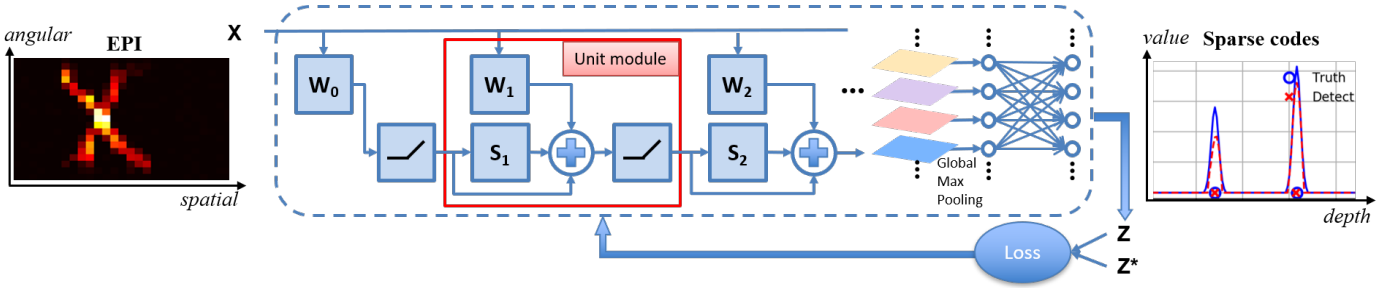
On-going work – CISTA for localization

- The convolutional sparse model leads naturally to an iterative optimization strategy (ISTA) that can be unfolded
- Training based on synthetic data obtained using the Broxton forward model



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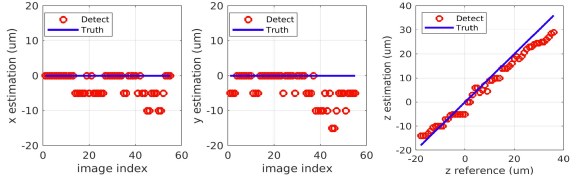
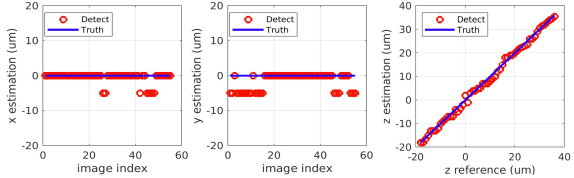
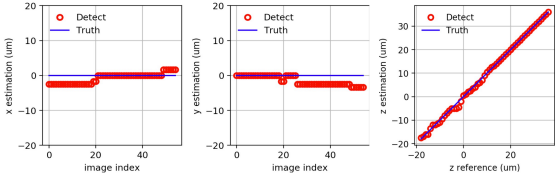
On-going work – CISTA for localization



(a) Localization performance of phase-space method [6, 8]. RMSE for x, y, z position detection is 4.05, 5.48, 3.41 μm, respectively.



(b) Localization performance of CSC approach [9]. RMSE for x, y, z position detection is 1.78, 2.94, 1.14 μm, respectively.



(c) Localization performance of the proposed CISTA-net. RMSE for x, y, z position detection is 1.60, 1.98, 0.82 μm, respectively.

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Conclusions

- Light field systems can have an impact in neuroscience because of the crucial trade-off between resolution in time and space
- Light field microscopy brings unique challenges e.g., wave optics
- In neuroscience applications, data is sparse and occlusion is negligible
- Understanding the physics of the problem is crucial
- Learning will labelled data is challenging

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Thank you!

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References

On Light-Field Microscopy and Neuroscience

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- H. Verinaz Jadan, P. Song, C. Howe, A. Foust and P.L. Dragotti, “Artifact-free 3D Reconstruction for Light Field Microscopy”, IEEE Transactions on Computational Imaging, submitted 2021.

- P. Song, H. Verinaz Jadan, C. Howe, P. Quicke, A. Foust and P.L. Dragotti, Light-field microscopy for optical imaging of neuronal activity, IEEE Signal Processing Magazine, submitted 2021.