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AI for Scientific Imaging

Pier Luigi Dragotti, Imperial College London

14 April 2026

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Motivation

- Inverse problems involve reconstructing unknown physical quantities from indirect measurements
- Recently we have witnessed a shift towards using data-driven methods to address inverse problems
- In this talk, I highlight advantages and pitfalls of data-driven solutions in imaging for scientific discovery

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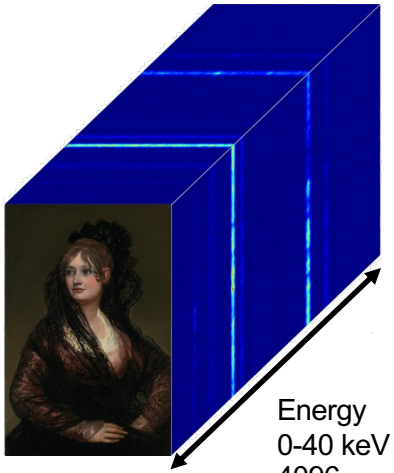
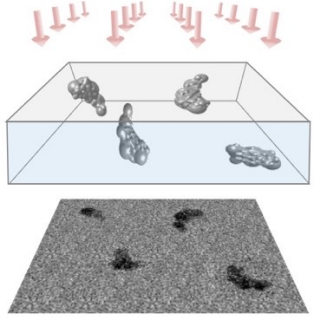
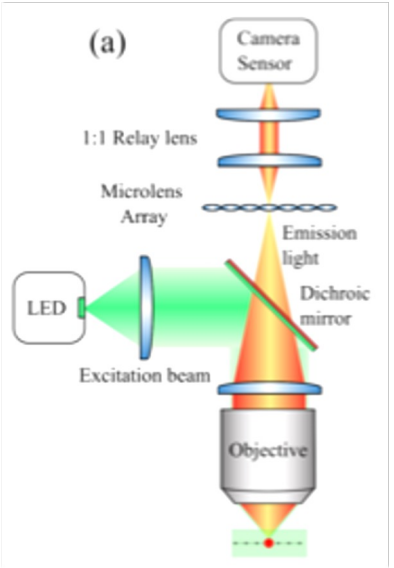
What do I do for a living: Inverse Imaging Problems



Technical study of Old Masters paintings



Cryo-EM for structural biology



Light field microscopy for neuroscience

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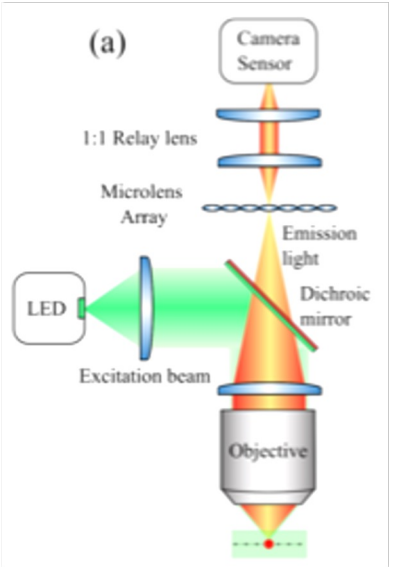
Scientific Imaging

Imaging for scientific discovery:

- Very complex imaging workflows
- No or limited ground truth data (but ever increasing size of data output)

- The growing complexity of modern imaging workflows calls for a more **holistic** approach to inverse problems where sensing, physics and computation are analysed jointly
- The lack of ground-truth data and large size of data output calls for methods that find the right **balance** between **data** and **priors**



Light field microscopy for neuroscience

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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
- Multi-photon microscopy combined with right indicators is the most promising technology to achieve that

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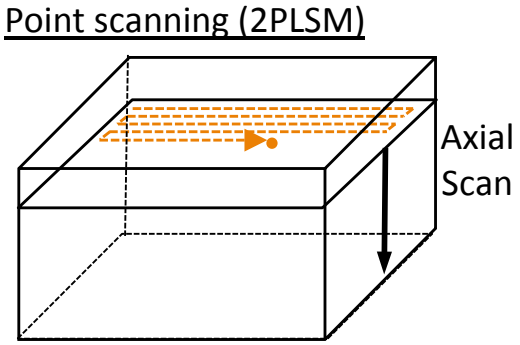
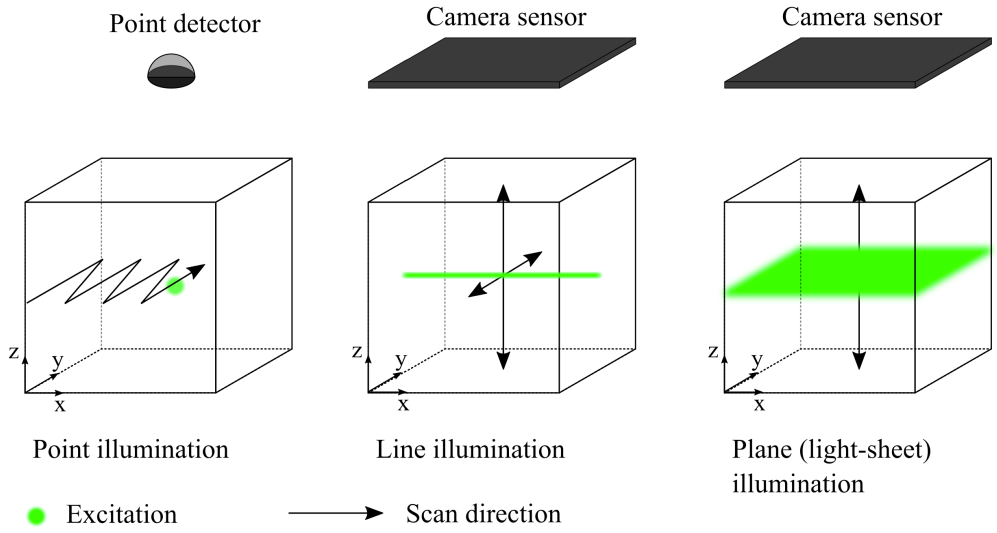
Two-Photon Microscopy

- 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
- Two-photon microscopes in raster scan modality can go deep in the tissue but are slow



Two-Photon Microscopy

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



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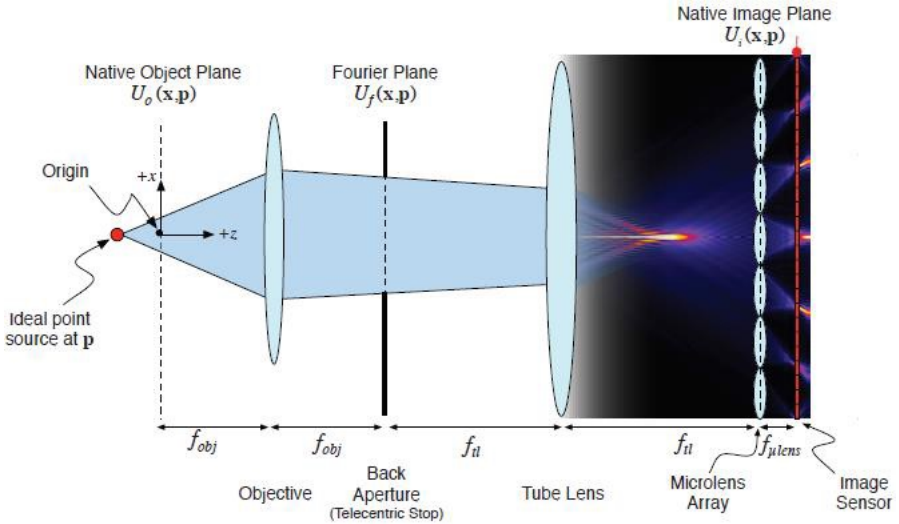
Light-field Microscopy

Light-Field Microscopy (LFM) is a high-speed 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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Lightfield vs Multi-Camera Systems

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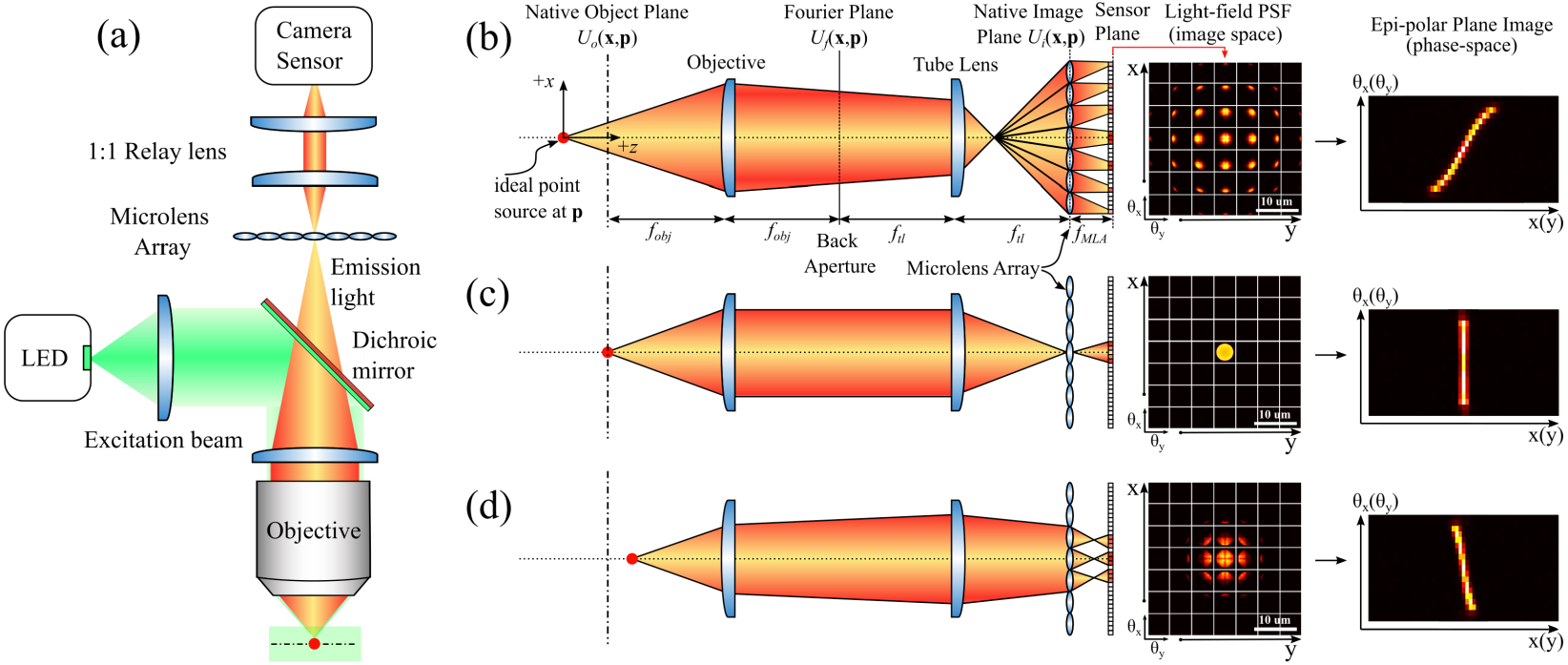
Light-field Microscopy and EPI



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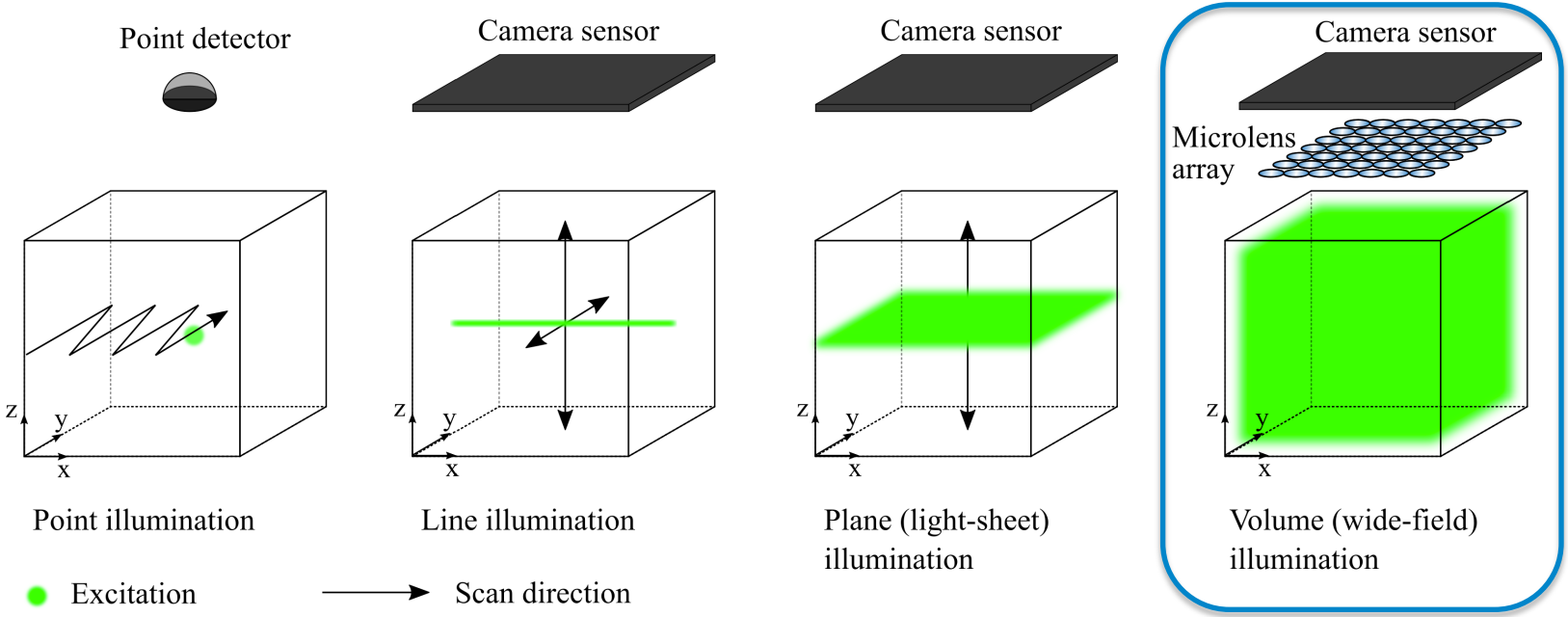
Light-field Microscopy and Illumination Strategies



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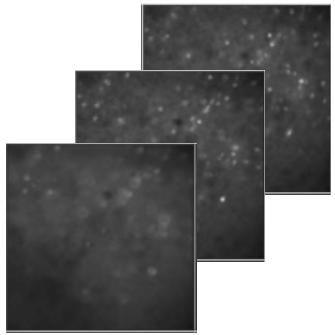
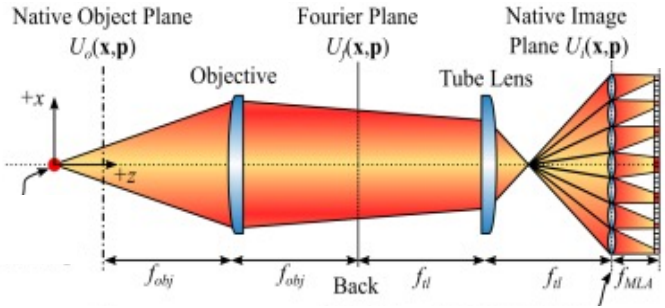
Light-field Microscopy

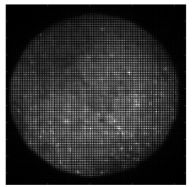
Challenge: given a sequence of lightfields (2-D signals), need to reconstruct a sequence of volumes (3-D+t)



3D Input



Computational Algorithm



2D Measured LF image

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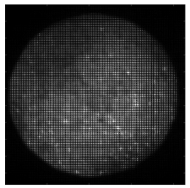
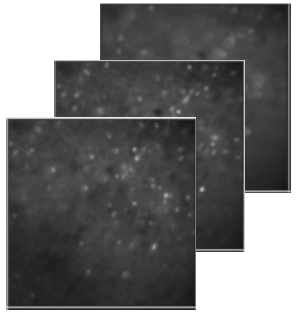
Volume Reconstruction from Light-field Data

- **Challenges**
  - Scattering induces blur, making inversion more challenging
  - Lack of ground-truth data for learning
- **Opportunities**
  - Forward model structured and linear
  - Data is sparse (neurons fire rarely and are localized in space)
  - Occlusion can be ignored



2-D LF



Volume

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Neural Network for Volume Reconstruction

- Data is sparse (neurons fire rarely and are localized in space)
- Solve $\min_x(\|y - Hx\|^2 + \|x\|_1)$ s.t $x \geq 0$
- This leads to the following iteration:

$$x_{k+1} = ReLU(x_k - H^T H x_k + H^T y + \lambda)$$

- Approach: Convert the iteration in a deep neural network using the ***unfolding technique***

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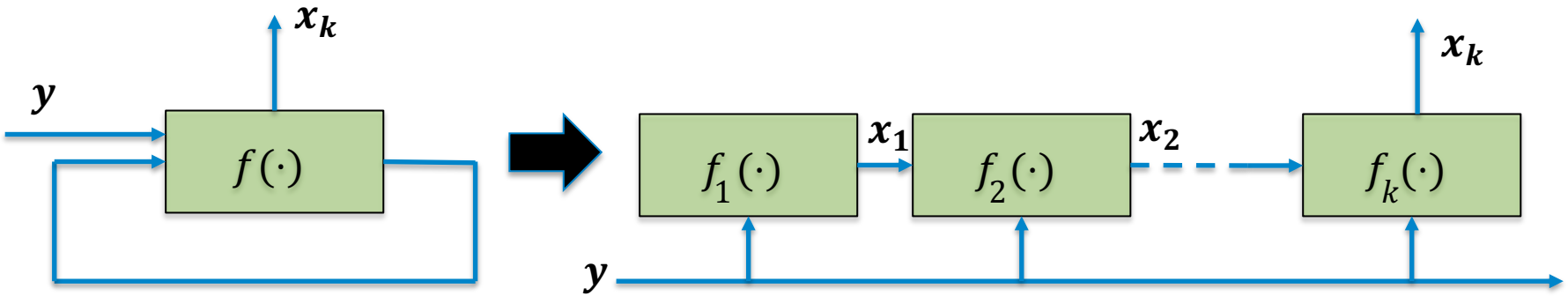
Sparsity and Deep Unfolding Strategy

Explicit embedding of priors and constraints in deep networks



Iterative algorithm with y as input and x as output

Unfolded version of the iterative algorithm with learnable parameters

Y. Eldar et al, “Algorithm Unrolling: Interpretable, Efficient Deep Learning for Signal and Image Processing”, IEEE Signal Processing Magazine, 2021

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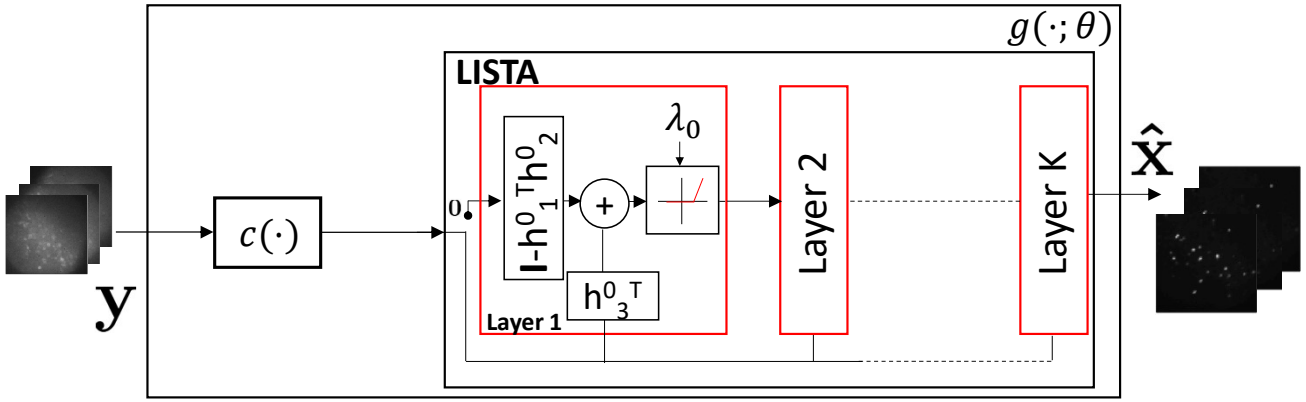
Neural Network for Volume Reconstruction

- Convert the iteration in a deep neural network using the unfolding technique

$$x^{k+1} = ReLU(x^k - H^T H x^k + H^T y + \lambda)$$



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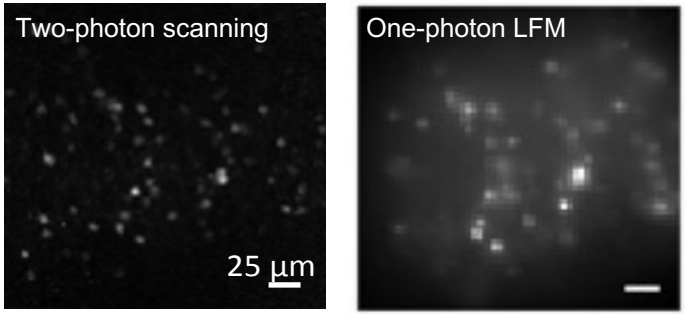
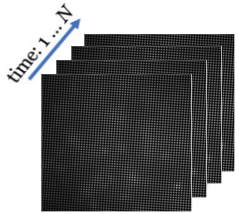
Our Solution: Scattering-robust structural volumes + high-bandwidth, scanless functional volumes

tdTomato structural marker



jGCaMP8f (world's fastest calcium indicator protein):
one-photon LFM at 100 Hz



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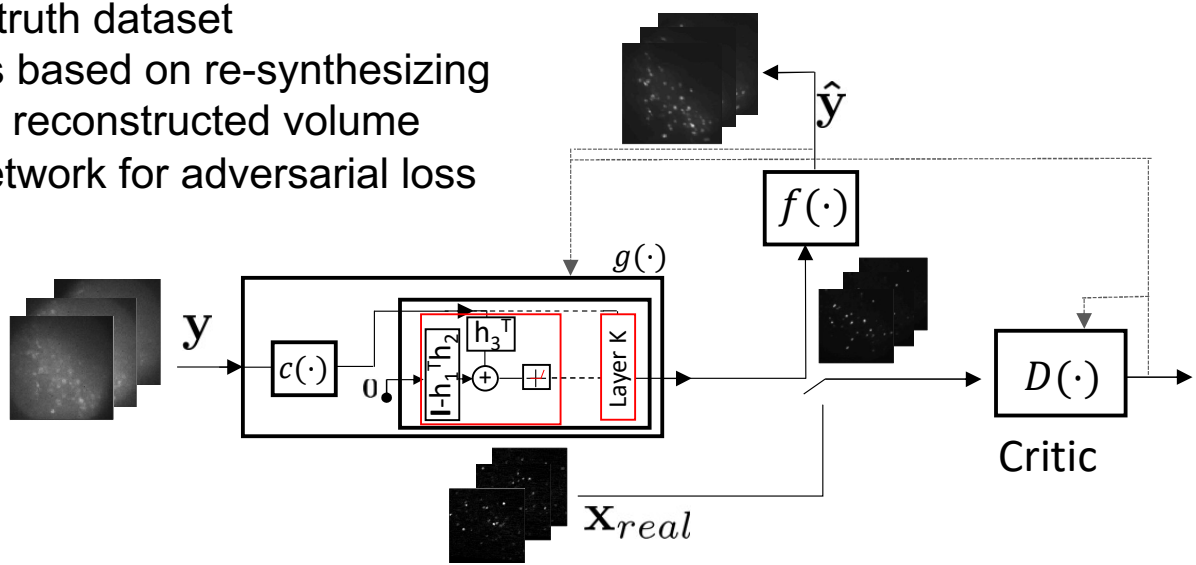
Training of the Neural Network

- Training, in this context, is difficult due to lack of ground-truth data
- Our approach: semi supervised learning
  - Small ground truth dataset
  - Light-field loss based on re-synthesizing light-field from reconstructed volume
  - Adversarial network for adversarial loss



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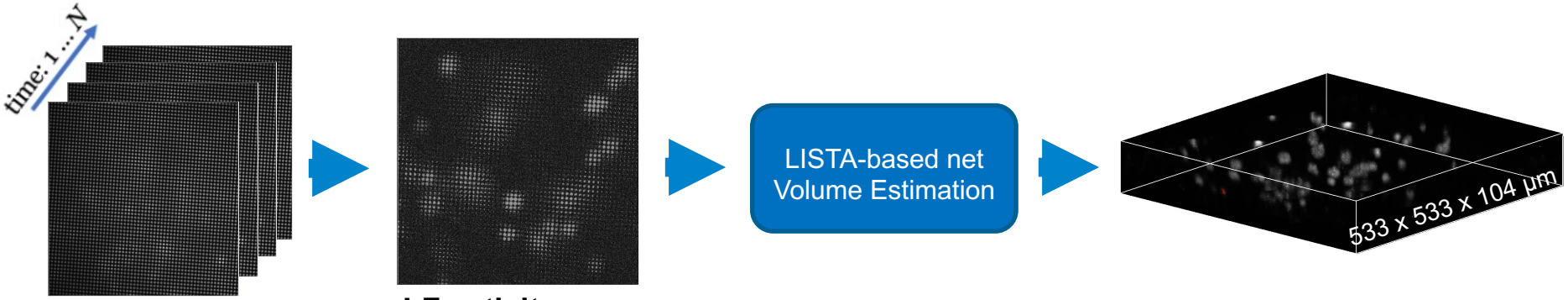
Fast volumetric jGCaMP8f time-series extraction



Input F(t):
LF video acquired in brain slice cortical layer 2/3

LF activity map:
max(ΔF)/σ(F)

H. Verinaz et al. "Physics-based Deep Learning for Imaging Neuronal Activity via Two-photon and Light-field Microscopy", IEEE Trans. on Computational Imaging, 2023.

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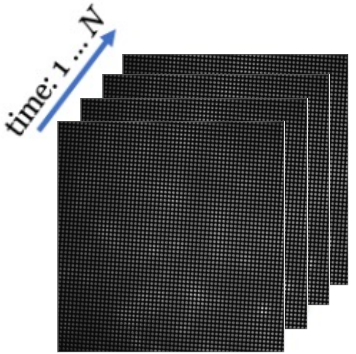

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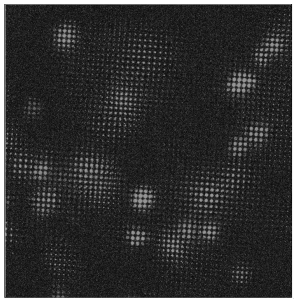
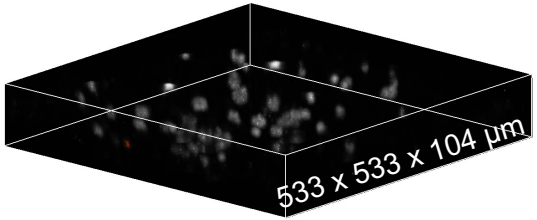
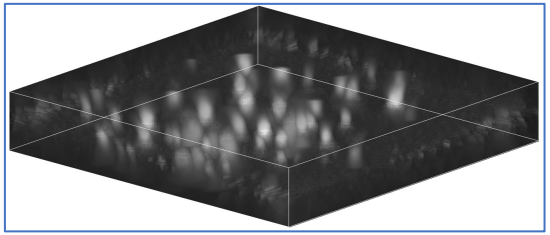


LF activity map:
max(ΔF)/σ(F)

LISTA-based net Volume Estimation



8-iteration Richardson-Lucy Deconvolution



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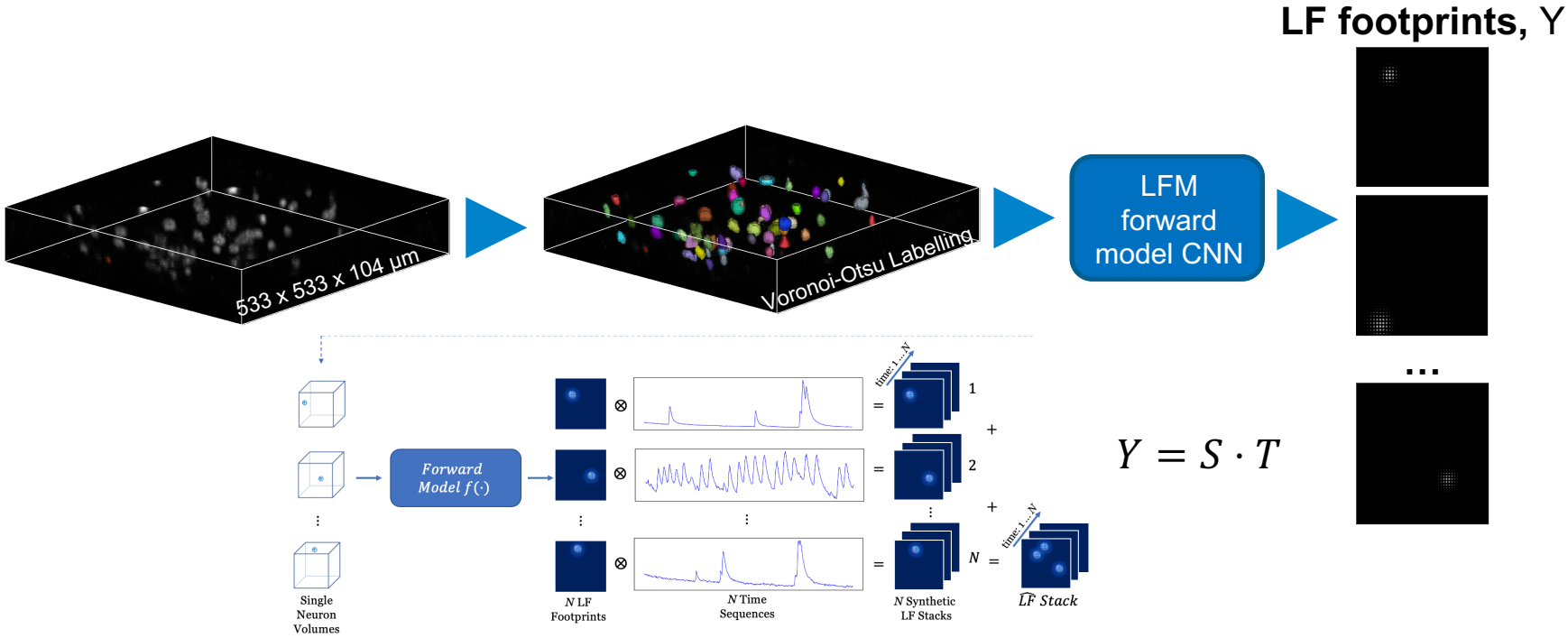

C. L Howe et al. "Light-field deep learning enables high-throughput, scattering-mitigated calcium imaging", Proceedings of the National Academy of Sciences (PNAS), 122 (48), 2025

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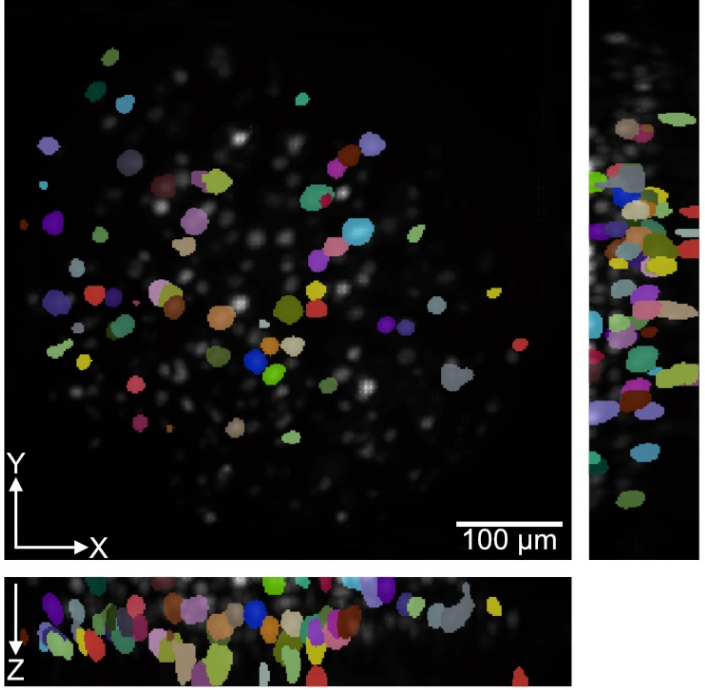

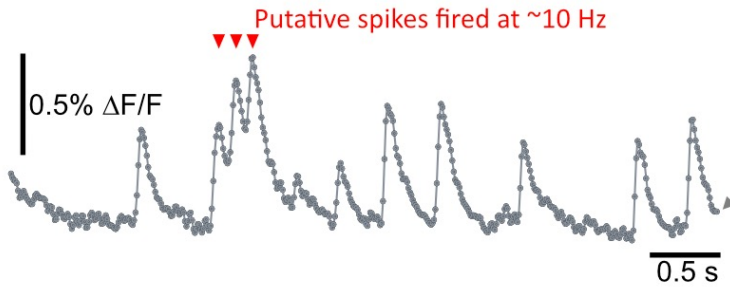

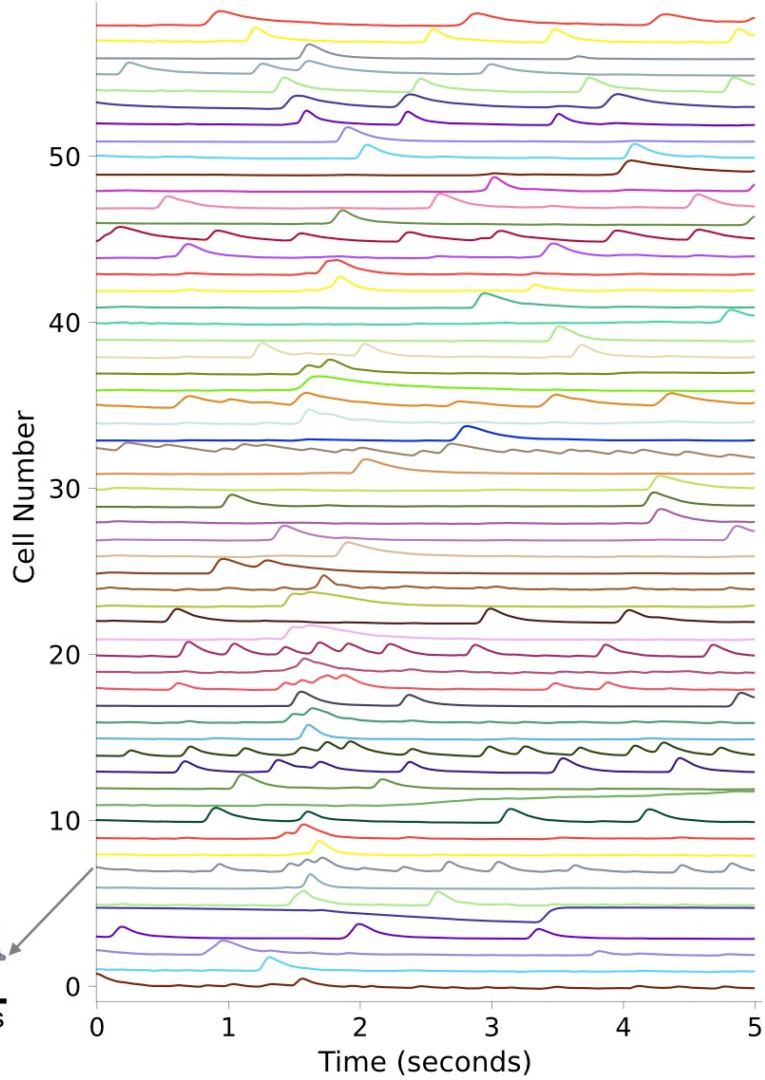

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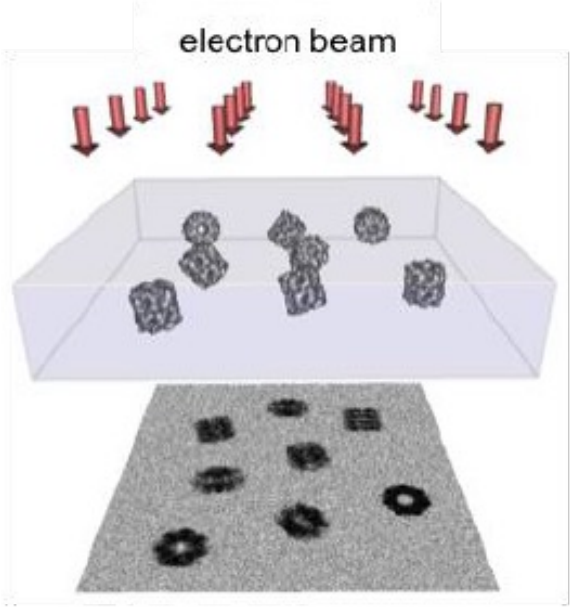
Electron Cryogenic Microscopy (Cryo-EM)

Electron Cryogenic Microscopy (Cryo-EM)

- A technique that allows the study of molecule structures at near-atomic resolution:
  1. Purified sample that contains the same molecule are cooled to cryogenic temperature and embedded in a thin layer of vitreous ice
  2. Parallel electron beams penetrate the sample, and we obtain a 2-D micrograph containing the tomographic projections of the molecules



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Open Questions

Since we cannot control how the molecule are oriented inside the sample, the micrograph effectively contains millions of 2-D projections of the molecule at random orientations. Open questions:

- **Uniqueness of the solution**: under what conditions can the original 3D structure be perfectly reconstructed from its filtered and sampled 2D projections?
- **Minimum number of projections**: how many projections are required to achieve perfect reconstruction?
- **Any constructive algorithms?**

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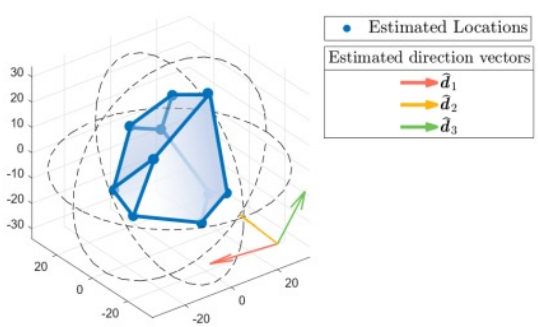
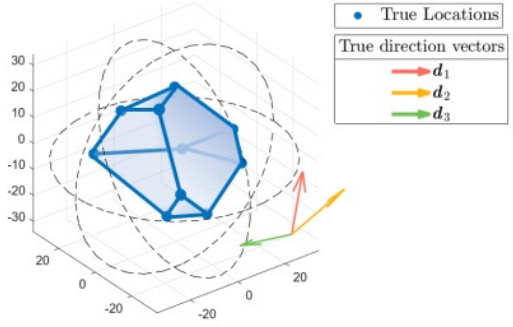
Perfect Reconstruction with Noiseless Samples



(a)



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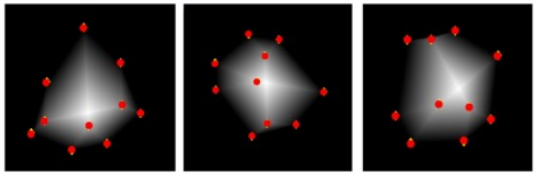

(c)

K. Zhao, R. Wang and P.L. Dragotti, “Reconstructing 3-D FRI shapes from tomographic projections at unknown angles”, International Conference on Sampling Theory and Applications (SampTA), 1-5, 2025

R. Wang and P.L. Dragotti “Perfect Reconstruction of Classes of 3D Non-Bandlimited Signals from Tomographic Projections at Unknown Angles”, European Signal Processing Conference (EUSIPCO), 2023

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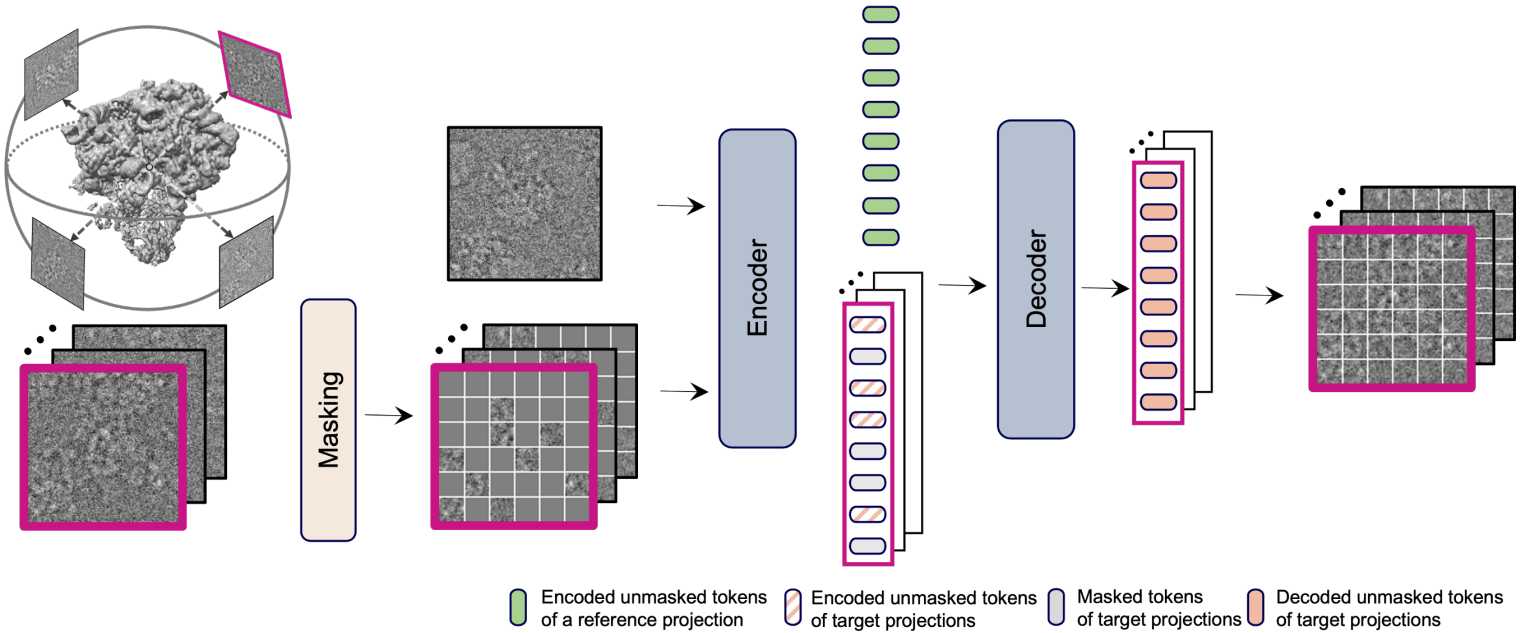
Masked Autoencoder to Estimate Orientation



J. Chen et al., Masked Projection Modelling for sparse-view Cryo-EM Reconstruction, IEEE ICASSP, 2026

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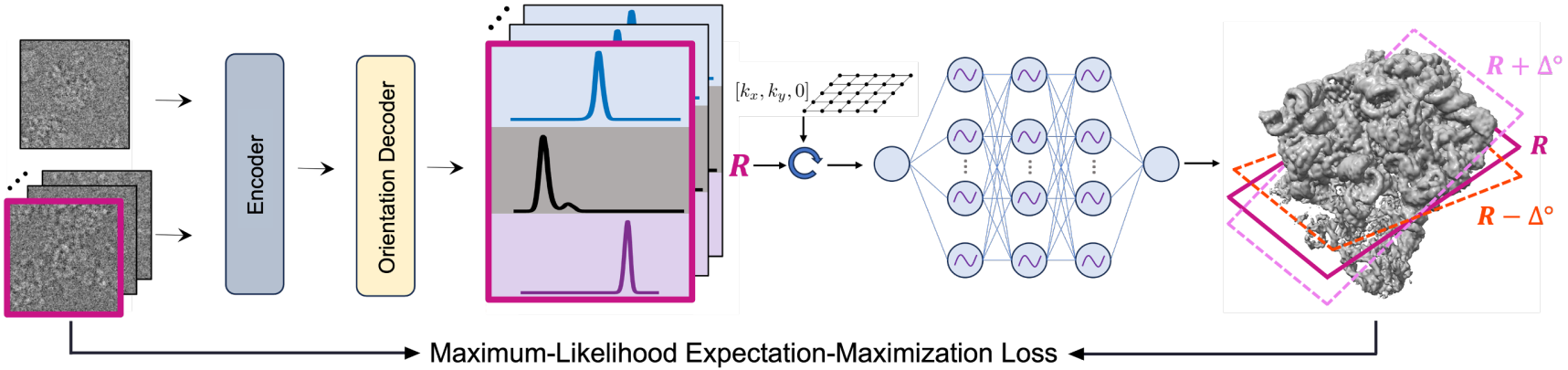
End-to-End Reconstruction Approach



J. Chen et al., Masked Projection Modelling for sparse-view Cryo-EM Reconstruction, IEEE ICASSP, 2026

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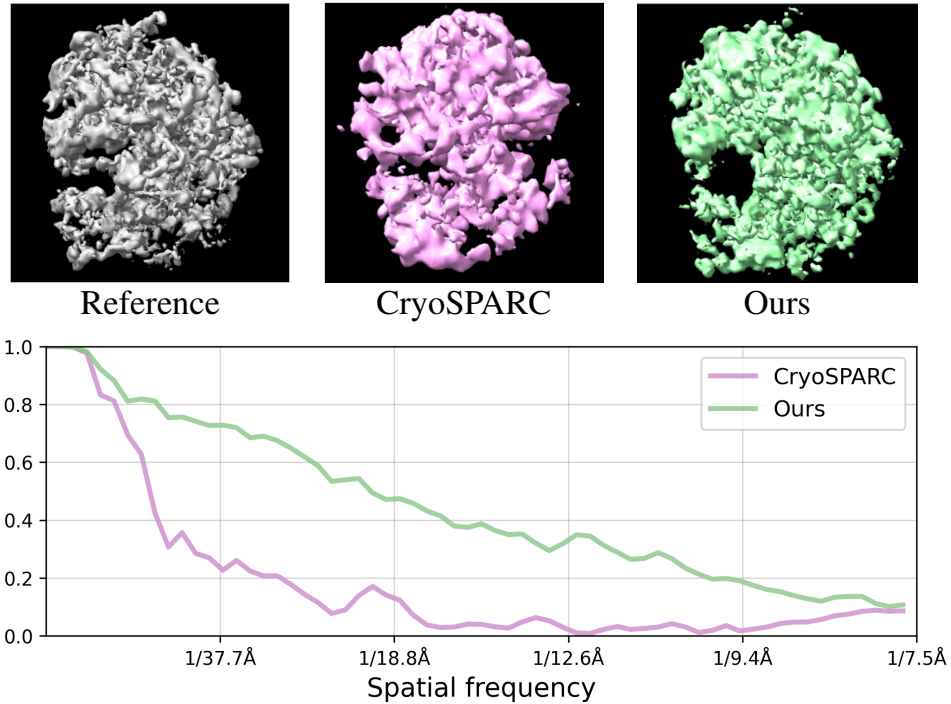
Reconstruction Results



J. Chen et al., Masked Projection Modelling for sparse-view Cryo-EM Reconstruction, IEEE ICASSP, 2026

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Conclusions

- In imaging problems:
  - operating at the interface between maths/physics and computation is essential
  - Cross fertilization between model-based approaches and deep learning is fruitful

- Inverse imaging problems:
  - are fun 🙂
  - and inter-disciplinary

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Special thanks to:

Kate Zhao

Pingfan Song

Peter Quicke

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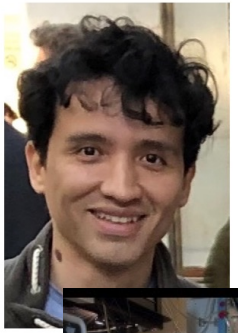
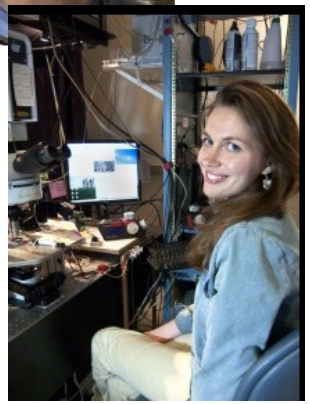
Herman Verinaz





Renke Wang

Doryen Bubeck

Amanda Foust

Thierry Blu

Jiakang Chen

Vincent Leung

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Thank you!

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Related Publications

- Cryo-EM:
  - K. Zhao, R. Wang and P.L. Dragotti, “Reconstructing 3-D FRI shapes from tomographic projections at unknown angles”, International Conference on Sampling Theory and Applications (SampTA), 1-5, 2025
  - R. Wang and P.L. Dragotti “Perfect Reconstruction of Classes of 3D Non-Bandlimited Signals from Tomographic Projections at Unknown Angles”, 31st European Signal Processing Conference (EUSIPCO), 1903-1907, 2023
  - J. Chen et al., Masked Projection Modelling for sparse-view Cryo-EM Reconstruction, IEEE ICASSP, 2026

- Light-field Microscopy:
  - H. Verinaz et al. "Physics-based Deep Learning for Imaging Neuronal Activity via Two-photon and Light-field Microscopy”, IEEE Trans. on Computational Imaging, 2023.
  - C. L Howe et al. “Light-field deep learning enables high-throughput, scattering-mitigated calcium imaging”, Proceedings of the National Academy of Sciences (PNAS), 122 (48), 2025