Deep neural network for SIM super-resolution reconstruction with a reduced number of images

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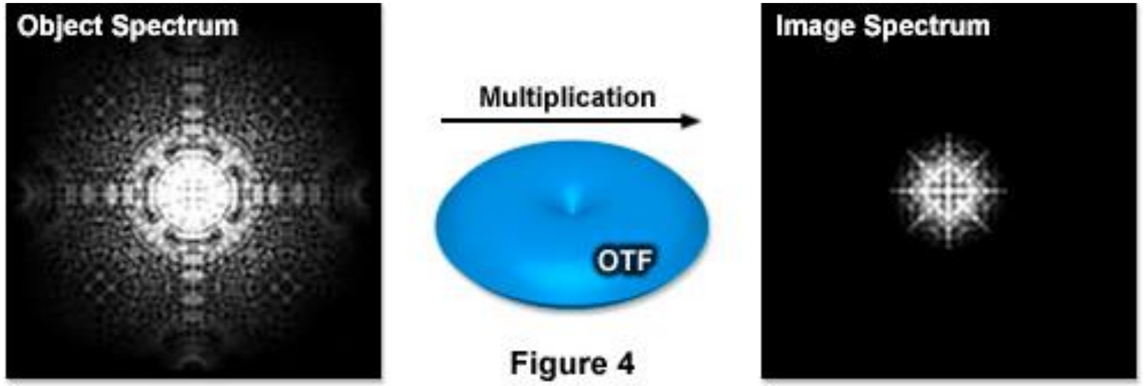
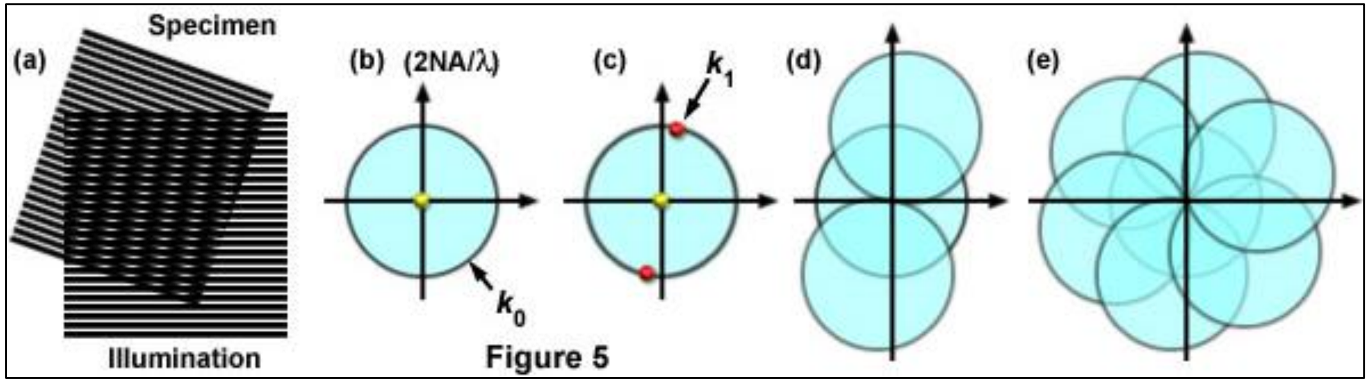
Super-Resolution Structured illumination microscopy (SR-SIM)

- Sinusoidal illumination pattern $I(r) = I_0[1 + \cos(k_0 \cdot r + \phi)]$
- Overcome diffraction limit ($\frac{\lambda}{2NA}$ or around 200nm)
- Mix high-frequency components into low-frequency components
- 9 images with 3 orientations x 3 phases

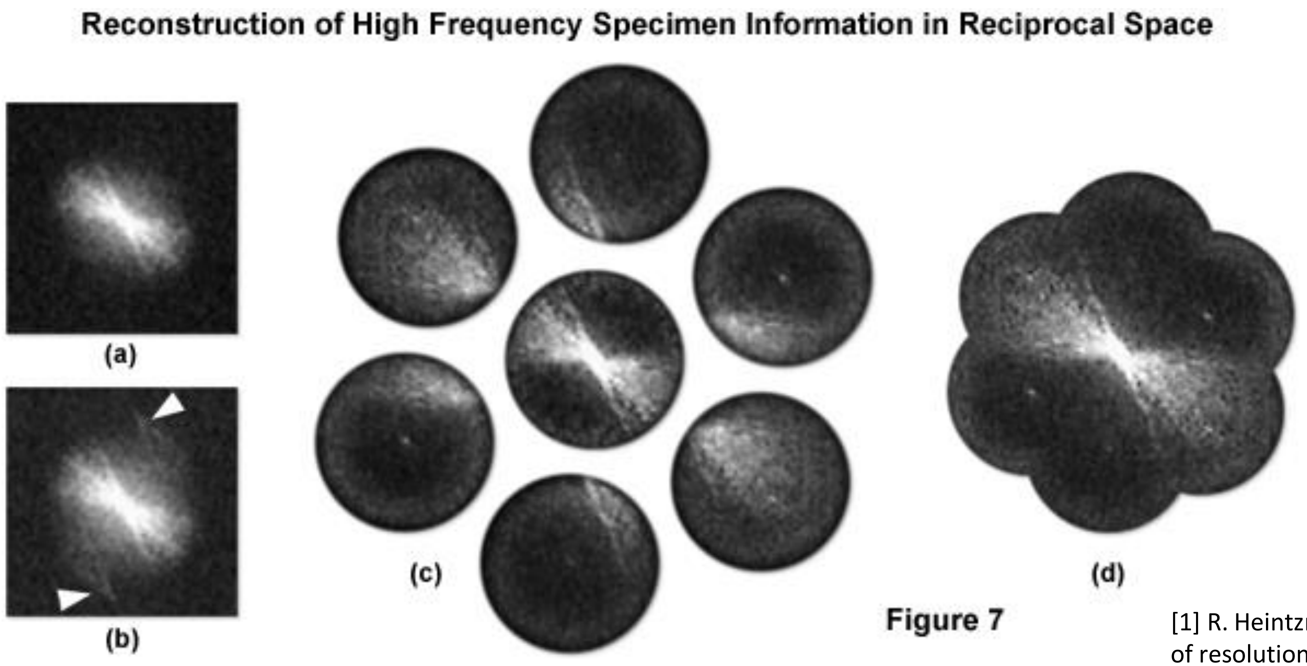


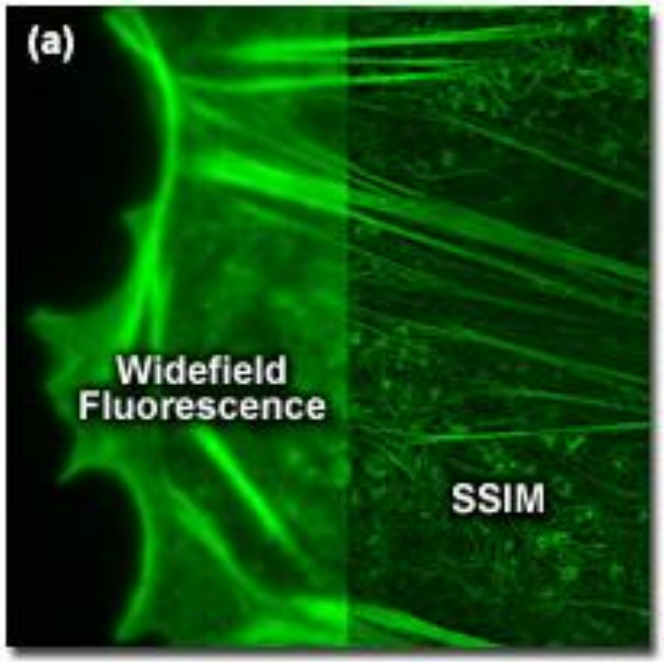


Source: http://zeiss-campus.magnet.fsu.edu/articles/superresolution/supersim.html

Direct method

- Using linear algebra to un-mix the Fourier components and create the composite Fourier Transform [1][2]
  - Pros: Good results, Reliable
  - Cons: Slow acquisition (9 images)
  - Cons: Can create unwanted artefacts in presence of noise





Source: http://zeiss-campus.magnet.fsu.edu/articles/superresolution/supersim.html

[1] R. Heintzmann and C. G. Cremer, “Laterally modulated excitation microscopy: Improvement of resolution by using a diffraction grating,” Proc. SPIE, vol. 3568, pp. 185–196, Jan. 1999.
[2] M. G. L. Gustafsson, “Surpassing the lateral resolution limit by a factor of two using structured illumination microscopy,” J. Microscopy, vol. 198, no. 2, pp. 82–87, Dec. 2001.

Using DNNs for SR-SIM : State of the art

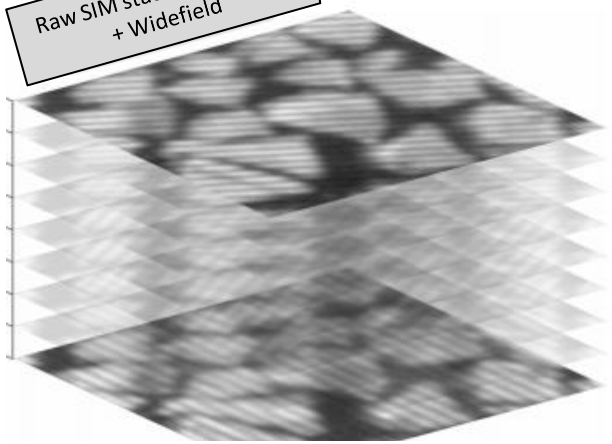
1. W2S [3]
   - Train a DNN to map a widefield (WF) image to a super-resolved SIM (SR-SIM) image
   - Pros: Fast acquisition (only one image, the WF)
   - Cons: unreliable as the input data (WF) do not contain high-frequency information
2. ML-SIM [4] or SR-REDSIM [5]
   - Train a DNN to reconstruct a SR-SIM from the raw data
   - Pros: physically relevant as the input data contains the high-frequecy info
   - Pros: can work with a reduced number of raw SIM images to accelerate acquisitions
   - Cons: Does not exploit the knowledge we have on how frequency components are mixed in SIM
3. RED-fairSIM [5]
   - Train a DNN to improve (artifact correction) the 9-images reconstruction obtained with FairSIM [6]
   - Pros: Exploits the knowledge we have on how frequency component are mixed in SIM
   - Pros: Significantly less sensitive to a change of system parameters between learning and testing
   - Cons: Slow acquisition (9 images)

[3] Majed El Helou, Daniel Sage, Thierry Laroche, Arne Seitz, Sabine Süsstrunk and W2Ruofan ZhouS, “Microscopy Data with Joint Denoising and Super-Resolution for Widefield to SIM Mapping”, ECCV 2020 Workshop on BioImage Computing, 2020
[4] Charles N. Christensen, Edward N. Ward, Pietro Lio and Clemens F. Kaminski, “ML-SIM: A deep neural network for reconstruction of structured illumination microscopy images”, University of Cambridge, 2020
[5] Zafran Hussain Shah , Marcel Müller , Tung-Cheng Wang , Philip Maurice Scheidig , Axel Schneider , Mark Schüttpelz , Thomas Huser , and Wolfram Schenck, “Deep-learning based denoising and reconstruction of super-resolution structured illumination microscopy images”
[6] Marcel Müller, Viola Mönkemöller, Simon Hennig, Wolfgang Hübner and Thomas Huser ,“Open-source image reconstruction of super-resolution structured illumination microscopy data in ImageJ”, Nature Communications, 2016

Could we get the best of both 2. and 3.?
→ This Project

- Exploit redundancy in 9-image SR-SIM
- Direct method using 4 images (3 orientations + Widefield)
    - It can be shown that 4 images (3 orr + 1 WF) contain all the frequency information needed for SR-SIM reconstruction
    - A direct reconstruction algorithm can be derived [See Semester project of Christophe Mueller, Fall 2018]
- Imperfect 4-image SR-SIM creates a lot of artefacts
- **Correct artefacts with DNN**

Raw SIM stack of 3 frames
+ Widefield



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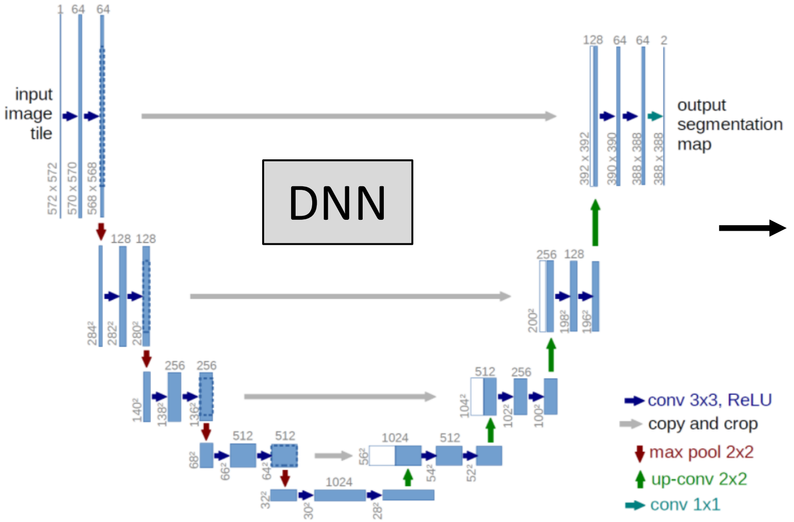
4-image SR-SIM reconstruction

→

DNN



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Super-Resolution image

DNN Structure / Training

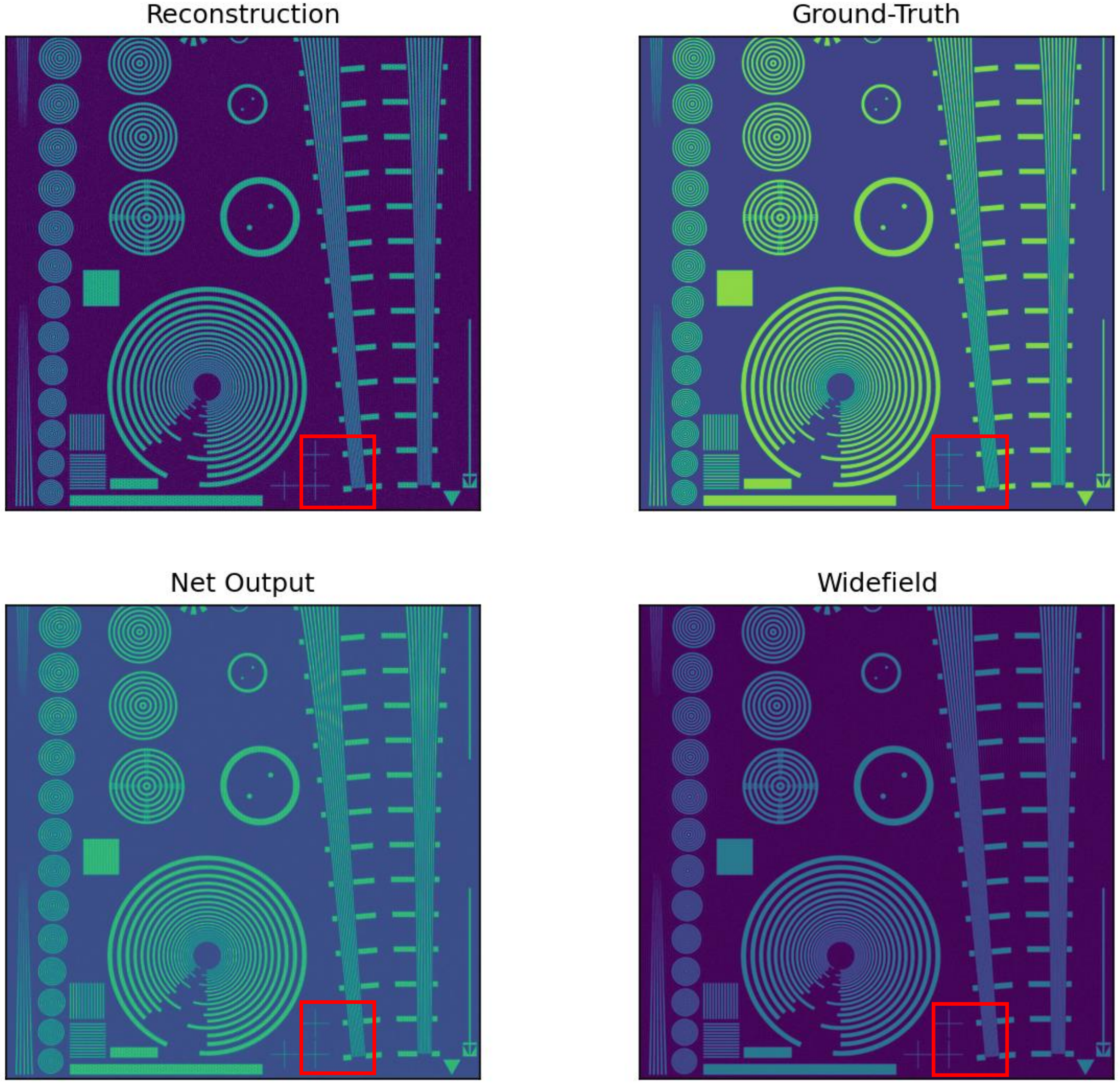
- "U-Net" structure
  - Convolutional Neural Net with several skip connections
  - Very memory-intensive (because of skip connections)
- Using a combination of L1 and SSIM loss
- At the moment using DIV2K dataset for training
  - 900 diverse **non-microscopy** images





- Input images are of size (1024x1024) and converted to grayscale, mean=0, std=1
- For a fair comparison all images are mapped to the range [0,1]

Intermediate Results: Generic Test Image



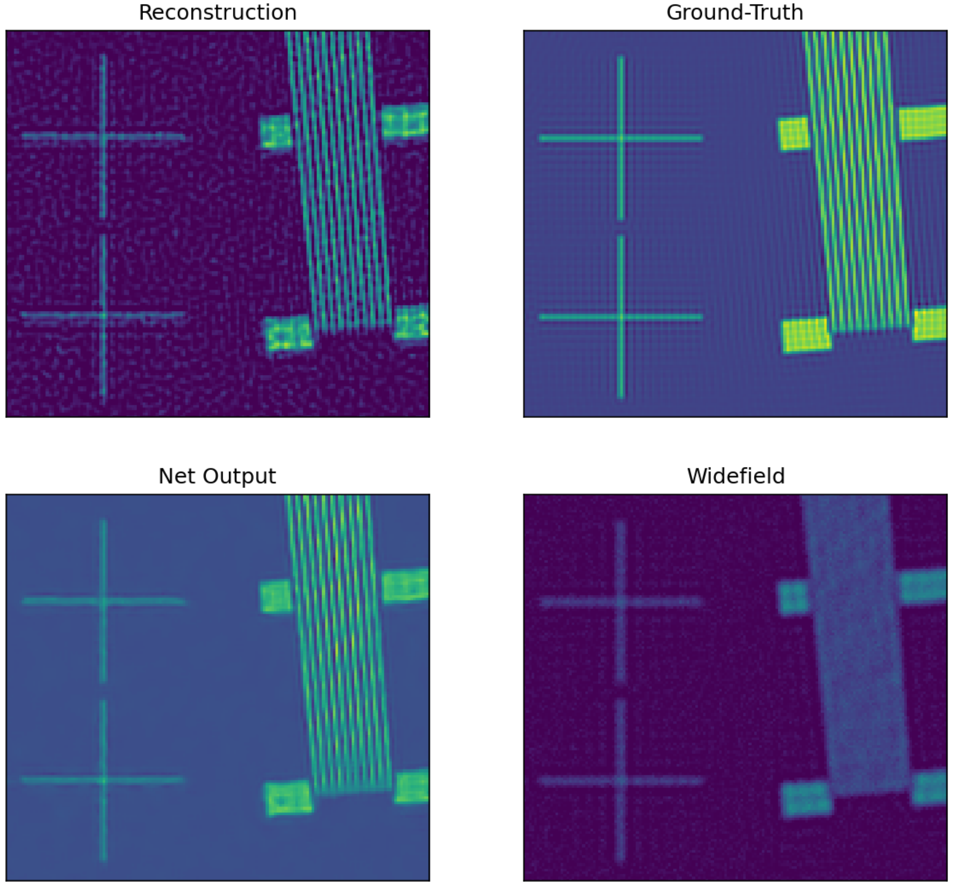
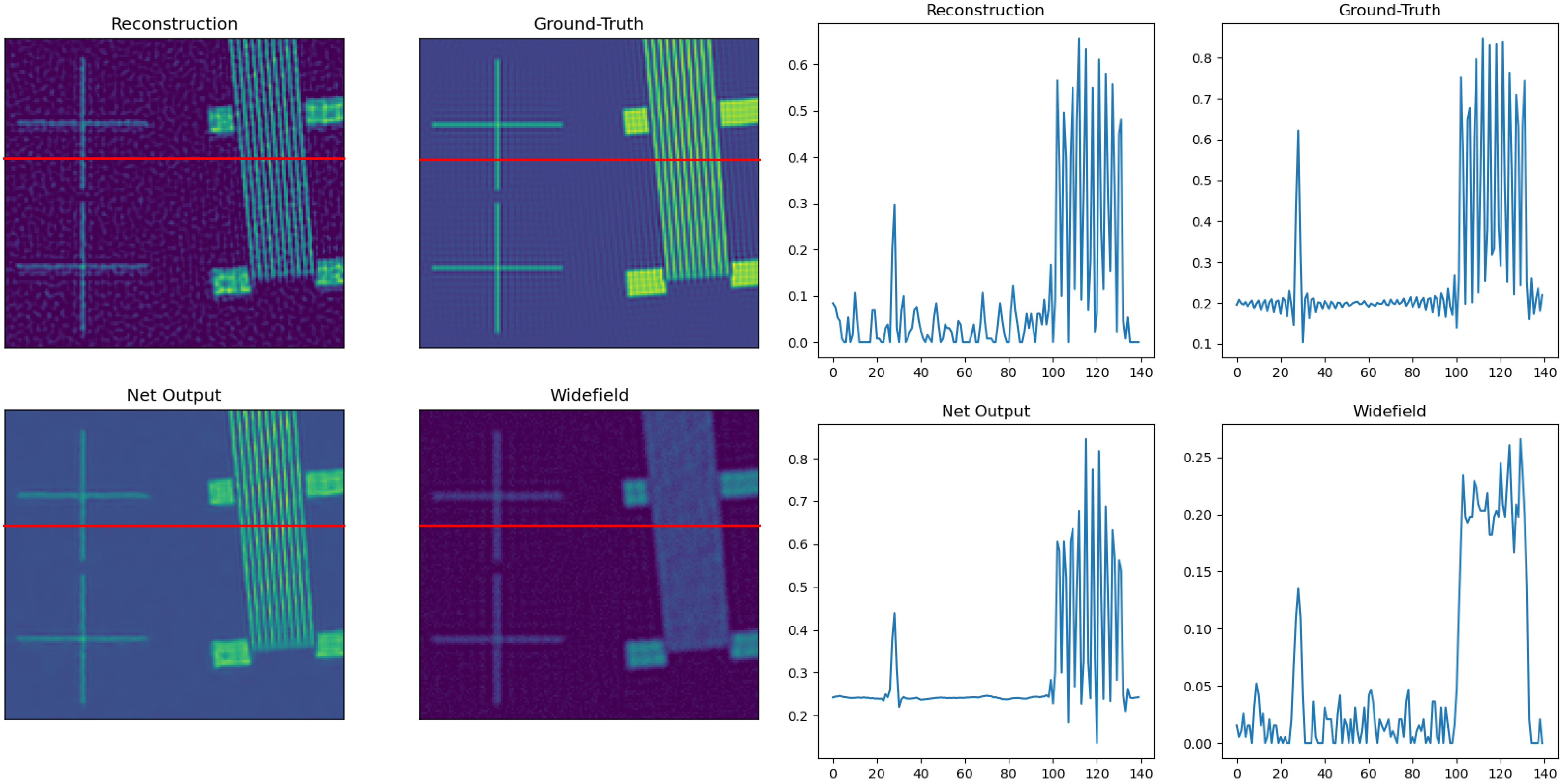
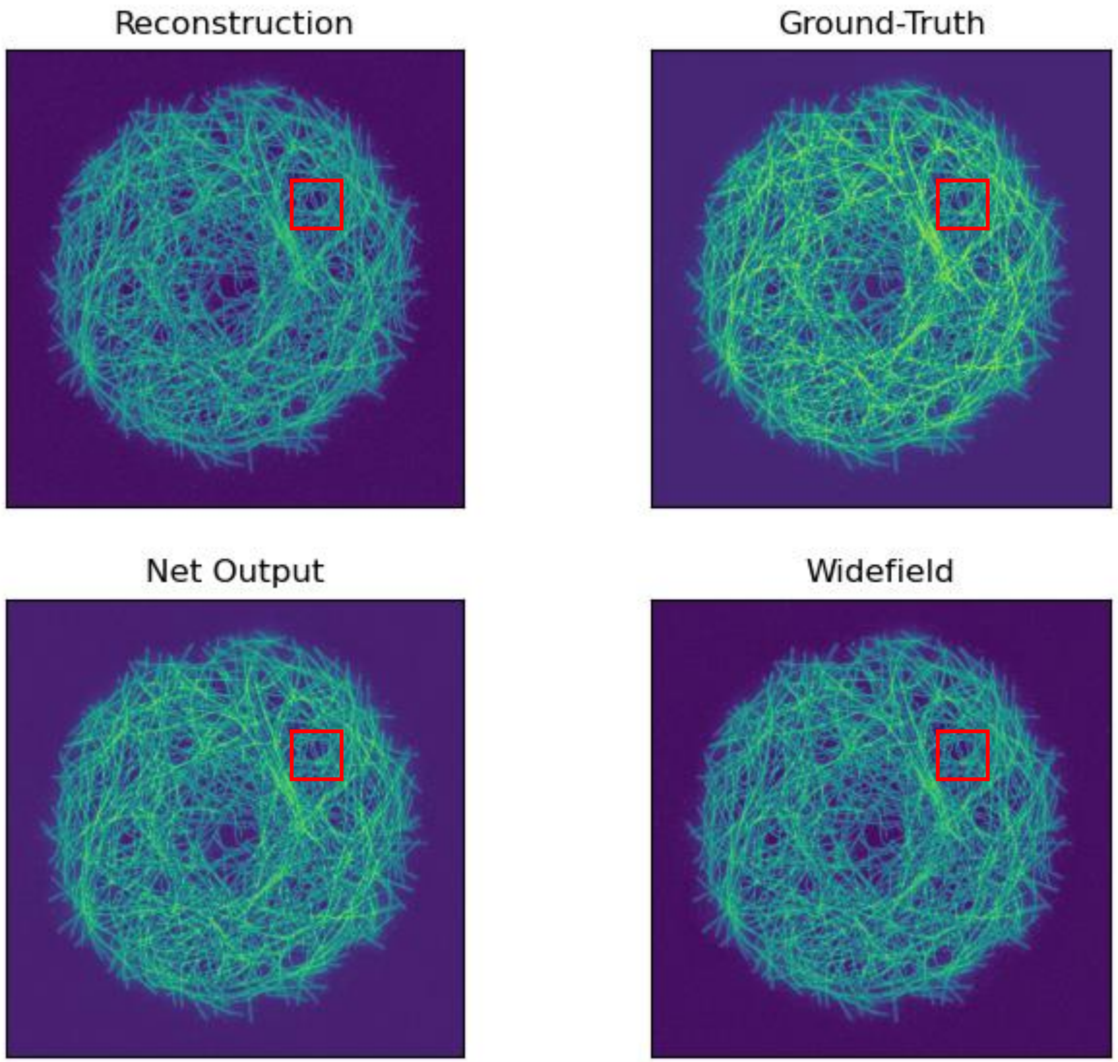


Image	SSIM	PSNR (dB)	SNR (dB)
Widefield	0.2829	11.3833	-1.4159
Reconstruction	0.4389	13.8177	-1.5872
Net output	0.9144	20.9013	3.0533
Ground Truth	-	-	1.4494


Reconstruction
Ground-Truth
Reconstruction
Ground-Truth
Net Output
Widefield
Net Output
Widefield

Intermediate Results: Microscopy Test Image



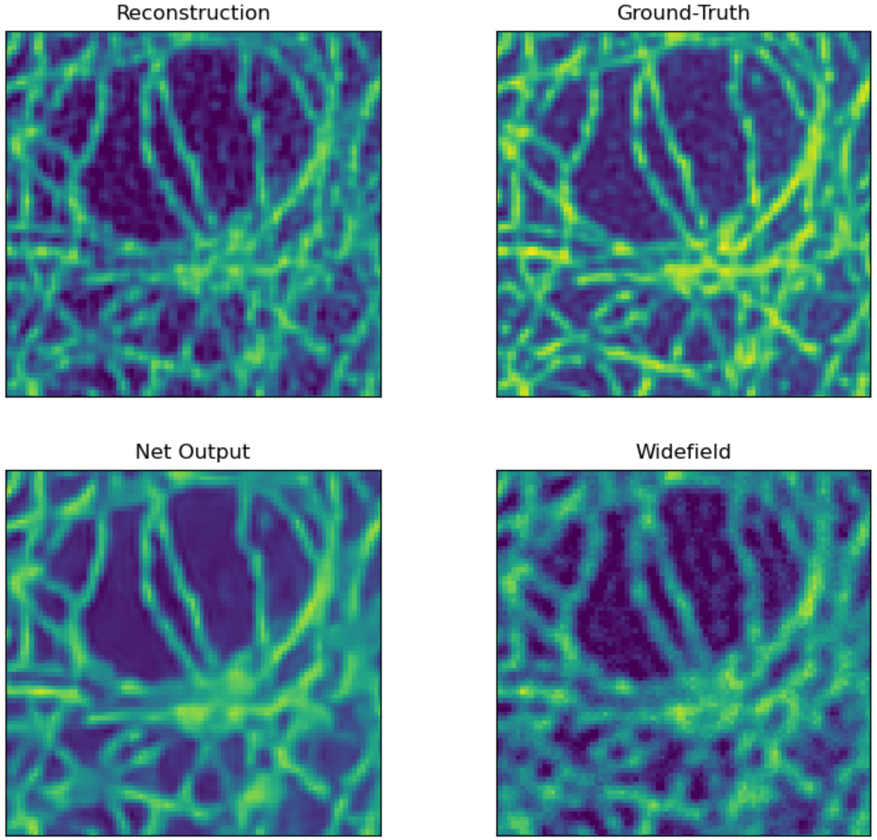


Image	SSIM	PSNR (dB)	SNR (dB)
Widefield	0.6977	20.383	-0.0263
Reconstruction	0.6796	19.9811	-0.0513
Net output	0.9265	24.7068	0.8221
Ground Truth	-	-	0.9351

Intermediate Results: Microscopy Test Image

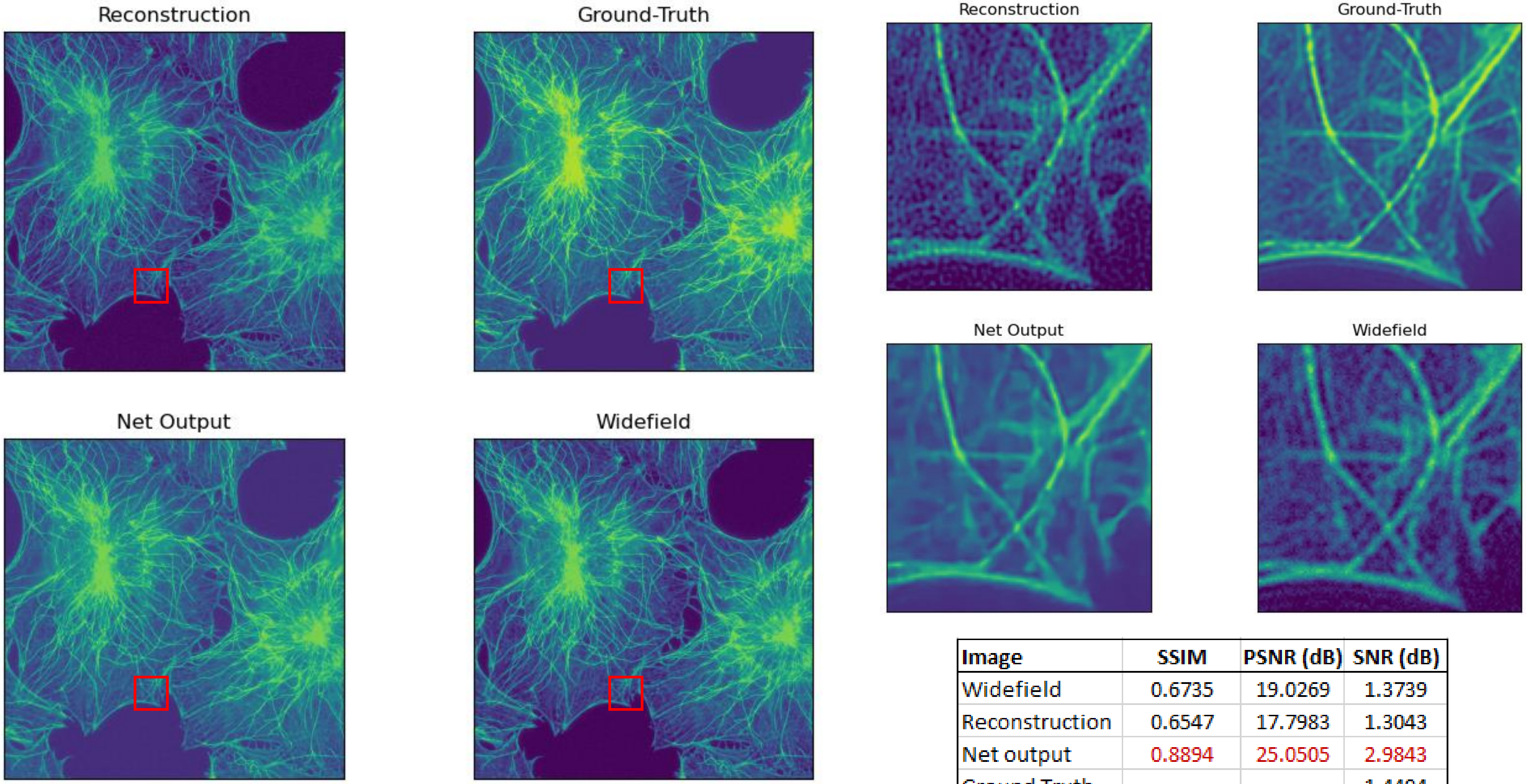


Image	SSIM	PSNR (dB)	SNR (dB)
Widefield	0.6735	19.0269	1.3739
Reconstruction	0.6547	17.7983	1.3043
Net output	0.8894	25.0505	2.9843
Ground Truth	-	-	1.4494

What’s next?

- Experiment with different noise levels (here SNR=20dB)
- Experiment with variations of loss function (weights for L1 and SSIM, here 0.16 and 0.84)
- Try RCAN network
  - Not as memory intensive
  - Could use Laplacian loss function that encourages high freq. correctness
- Train on microscopy images → dataset used by W2S (SIM would still be simulated)
- 4-image simulated SIM: use real PSF/OTF
- Train on real SIM data → no suitable dataset found

Discussion Time