Diffusion Models in Microscopy:
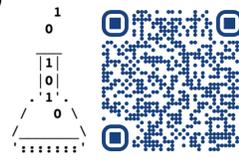# Bleedthrough Removal, Image Splitting, and Dehazing

Anirban Ray*[1,2], Ashesh Ashesh[1,2], and Florian Jug[2]
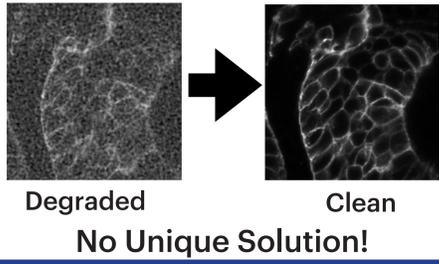[1]Human Technopole, Milan, Italy
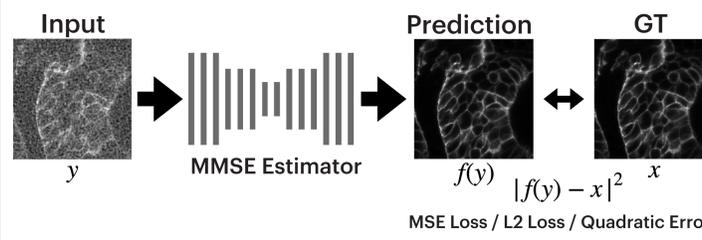[2]Technische Universität Dresden, Germany

I2K
From Images to Knowledge 2024

Background and Motivation

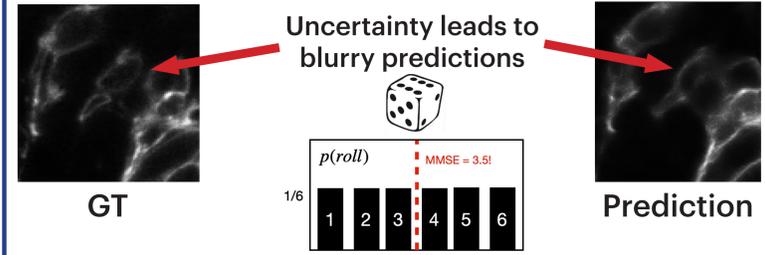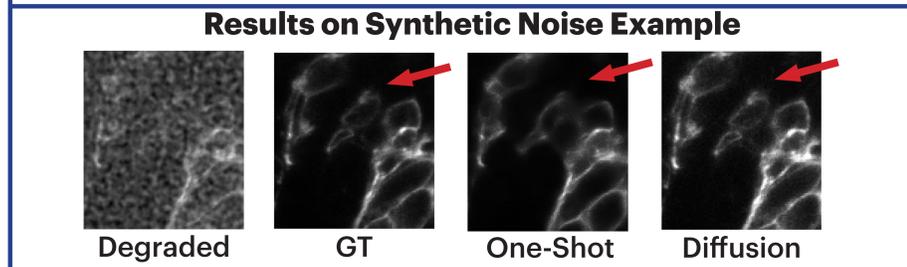**Restoration Tasks (Inverse Problem)**

Degraded — Clean
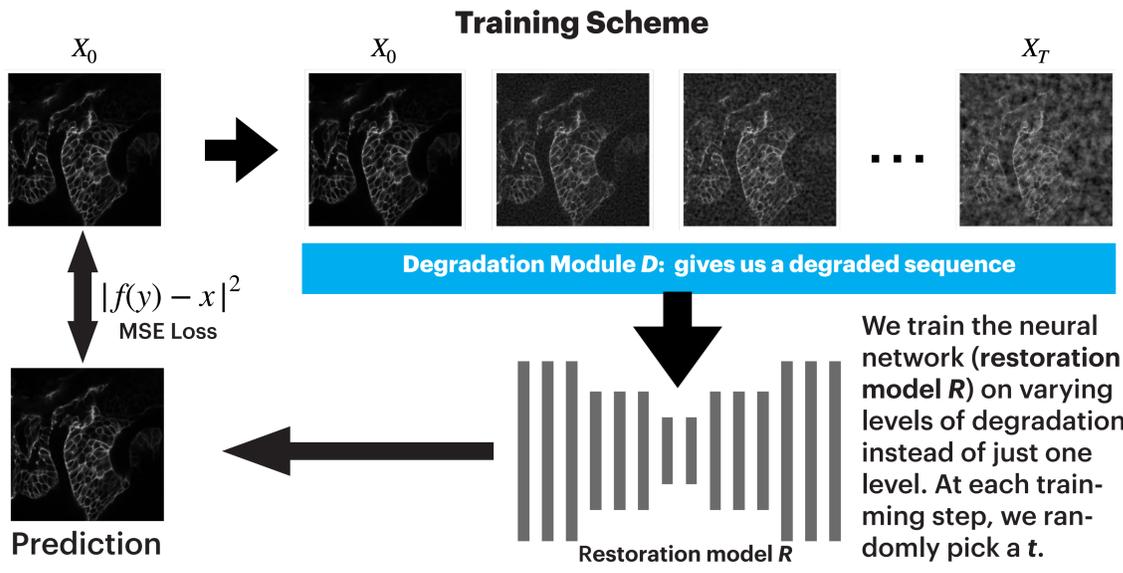No Unique Solution!

Traditional One-Shot Deep Learning Approach

Input y → MMSE Estimator → Prediction $f(y)$ ↔ GT x
$|f(y) - x|^2$
MSE Loss / L2 Loss / Quadratic Error

Regression-to-Mean Effect (Blurry Structures)
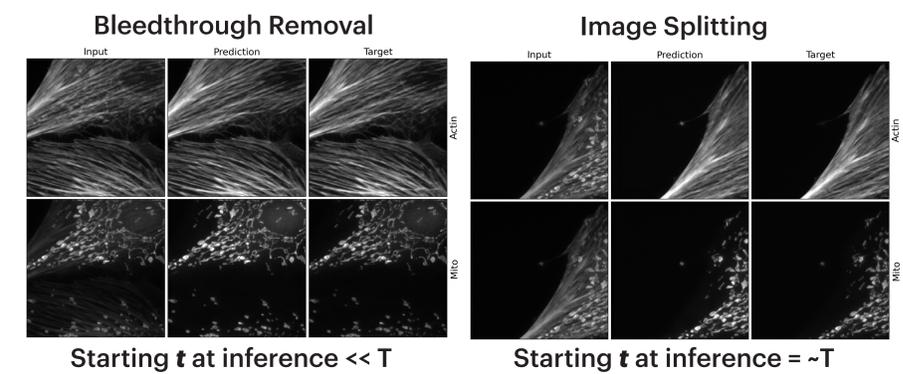

Uncertainty leads to blurry predictions
GT — Prediction
$p(roll)$ MMSE = 3.5!

Diffusion Models: an Iterative Approach

Training Scheme

X_0 ... X_0 ... X_T

Degradation Module D: gives us a degraded sequence

$|f(y) - x|^2$
MSE Loss

Prediction

We train the neural network (**restoration model R**) on varying levels of degradation instead of just one level. At each training step, we randomly pick a t.

Restoration model R

Iterative Inference

Degradation Module D ... X_{T-2} X_{T-1} X_T

Restoration model R

We use the neural net (R) and the degradation module (D) iteratively, to predict and degrade the prediction and return the final prediction after $T-2$ iterations.

Results on Synthetic Noise Example

Degraded — GT — One-Shot — Diffusion
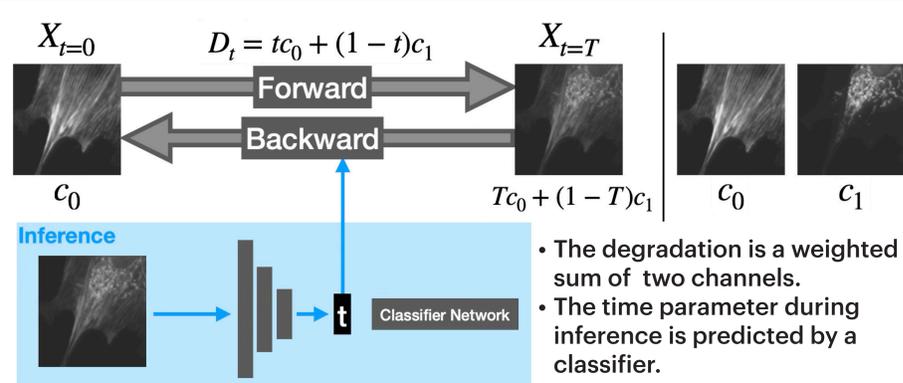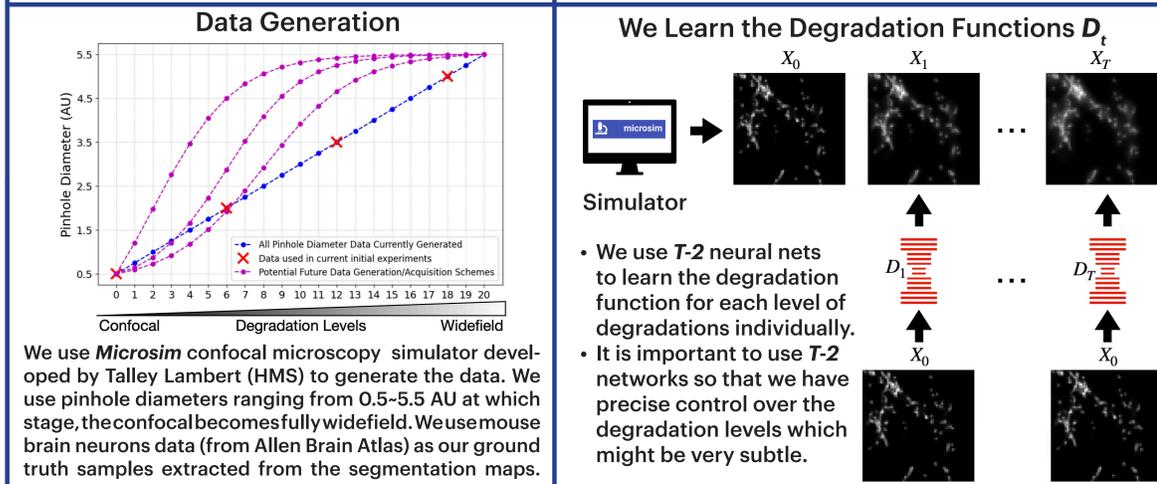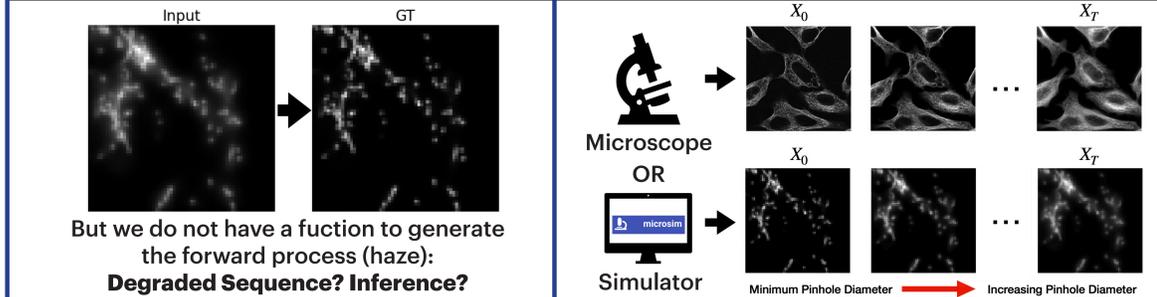
Applications to *Known* and *Unknown* Degradations in Microscopy Data

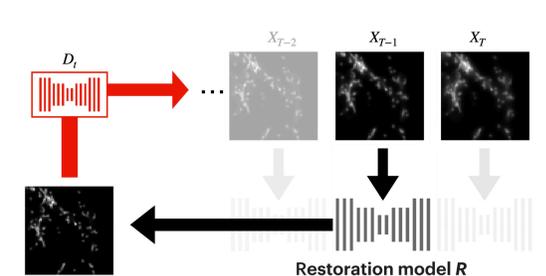### BLEEDTHROUGH REMOVAL AND IMAGE SPLITTING (*Known D*)

$X_{t=0}$ $D_t = tc_0 + (1-t)c_1$ $X_{t=T}$
Forward
Backward
c_0 $Tc_0 + (1-T)c_1$ c_0 c_1

Inference

Classifier Network

• The degradation is a weighted sum of two channels.
• The time parameter during inference is predicted by a classifier.

Bleedthrough Removal

Input — Prediction — Target
Actin
Mito

Image Splitting

Input — Prediction — Target
Actin
Mito

Starting t at inference $\ll T$ | Starting t at inference $= \sim T$

WIDEFIELD MICROSCOPY IMAGE DEHAZING (*Unknown D*)

Input — GT

But we do not have a fuction to generate the forward process (haze):
Degraded Sequence? Inference?

Microscope OR Simulator
X_0 ... X_T
Minimum Pinhole Diameter → Increasing Pinhole Diameter

Data Generation

Pinhole Diameter (AU)
Degradation Levels
Confocal — Widefield
— All Pinhole Diameter Data Currently Generated
✗ Data used in current initial experiments
- - - Potential Future Data Generation/Acquisition Schemes

We use **Microsim** confocal microscopy simulator developed by Talley Lambert (HMS) to generate the data. We use pinhole diameters ranging from 0.5–5.5 AU at which stage, the confocal becomes fully widefield. We use mouse brain neurons data (from Allen Brain Atlas) as our ground truth samples extracted from the segmentation maps.

We Learn the Degradation Functions D_t

X_0 X_1 ... X_T
Simulator
D_1 ... D_T
X_0

• We use $T-2$ neural nets to learn the degradation function for each level of degradations individually.
• It is important to use $T-2$ networks so that we have precise control over the degradation levels which might be very subtle.

Inference with Learned Degradation Functions

D_t ... X_{T-2} X_{T-1} X_T

Restoration model R

During the iterative inference, instead of a known degradation module, as in a normal case, we use the trained degradation neural networks to induce the desired level of degradation to the data. Note that the degradation networks expects clean images which are provided by the restoration model.

What makes a good Posterior?

X_T Full cycle iterative inference N Predictions (Posterior)
$\times N$ Restoration model R
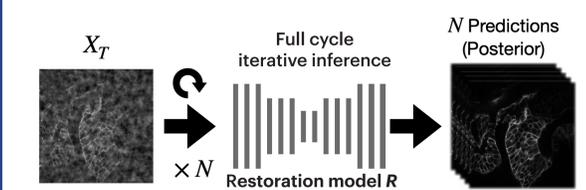
A posterior returns samples which are plausible (and not the MMSE). Therefore, the desired qualities of a posterior that we aim for are:
• MMSE of the posterior samples should match a one-shot MMSE estimator.
• The each sample in the posterior should be "in-distribution".
• Should be able to determine the uncertainty in the data by analyzing posterior samples.

Challenges

• **Out-of-distribution (OOD) during inference:** If the (R) is trained with T=GT(T) data, feeding T=D(T) during inference can cause performance drop due to OOD.
• **Taking advantage of the predicted posterior samples in downstream analysis:** How can we leverage the data uncertainty of the posterior to make downstream tasks better.

"Diffusion models can provide plausible restored solutions in an inverse problem, avoiding the averaging of all possible solutions."

References

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3. Kawar, et al. (2022). Denoising diffusion restoration models. In Oh, A. H., Agarwal, A., Belgrave, D., and Cho, K., editors, Advances in Neural Information Processing Systems.
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