Unsupervised Deep Denoising for High-Dimensional Microscopy Data

Leonardo Cancellara[1], William Talbott[2], Ankit Shrivastava[3], Jordi Weingard[2], Dingqiao Ji[1], Ian MacLaren[4]

[1]Max Planck Institute of Colloids and Interfaces,
[2]University of Manchester,
[3]Oak Ridge National Laboratory,
[4]School of Physics and Astronomy, University of Glasgow, Glasgow G12 8QQ, UK

Background

Recent advances in detectors have enabled a drastic reduction in electron dose during TEM and STEM observations, enabling analysis of highly beam-sensitive materials. In more extreme cases, such as biological materials and liquids, however, very low doses are still required, yielding noisy data. However, noise can be reduced with advanced post-processing, such as UDVD (Unsupervised Deep Video Denoising), a UNet-based CNN (Convolutional Neural Network) (Crozier *et al*., 2025), for denoising time-series image data, based on the hypothesis that subsequent frames share similar underlying data. The work has also been successfully applied to spatially adjacent frames of electron energy loss spectroscopy (EELS) data (Wang *et al.*, 2025). We exploit the fact that high-dimensional microscopy data, such as EELS and 4D-STEM, often exhibit underlying similarity between neighboring scan positions, enabling pixel-wise denoising of diffraction data by comparing to adjacent pixels. Furthermore, UDVD has the significant advantage that it requires no ground truth for the training.

Our system has two novelties that generalise Crozier's method. Firstly, we denoised a four-dimensional set of data (4D-STEM) rather than typical STEM data, using an approach that can be generalised to higher dimensions. Secondly, we used geometric-flow data that connect related frames via real-space geometry rather than temporal positions.

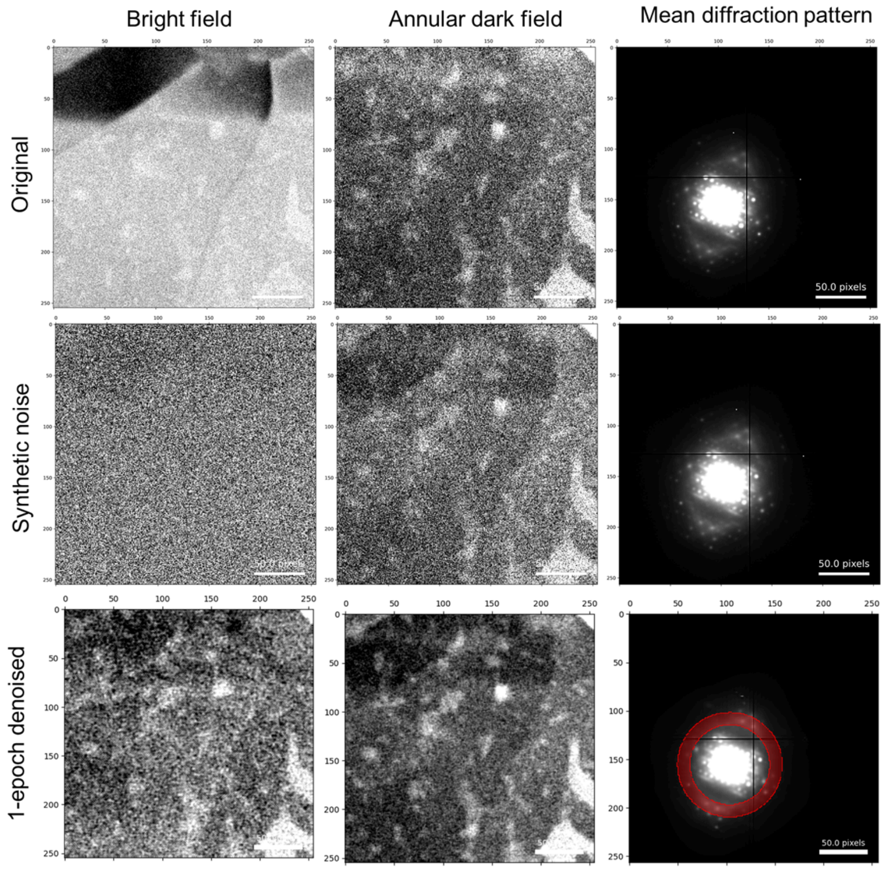
To demonstrate the potential of unsupervised denoising, we created a semi-synthetic nanobeam 4D-STEM dataset by adding controlled noise models to open-source experimental data from Pham *et al*. (2025). These low-dose datasets of beam-sensitive materials could then be used to both train and test our denoiser. Denoising data is beneficial, as SNR improvements enable improved nano-resolved crystallographic characterisation with reduced dose and thus reduced radiolysis damage. Pham *et al*. (2025) also showed dislocations in these molecular crystals via 4D-STEM analysis, and denoising lower-dose data would extend that benefit to even more beam-sensitive materials.

Methodology

UDVD was initially designed for video denoising using time-series frames; extending it to multidimensional microscopy datasets, such as 4D-STEM, required modifying the data representation so that the model could operate on geometric-flow data. This was done using a custom dataloader that prepared them for input into the neural network. For each position, it created a 5-frame stack from 4 neighboring positions plus the center. This required avoiding the edges to ensure that all processed pixels had the same number of neighbours used in the denoising.

We initially used Crozier *et al.'s* pre-trained model weights to verify that the model worked, then trained it on the data from Pham *et al*. (2025). We trained with approximately 50000 datasets to denoise the diffraction pattern at a scanning location. Due to time and resource constraints, only one epoch was used for training; performance is expected to improve with more epochs. The UDVD architecture uses standard Python libraries to create the model architecture (PyTorch) and for GPU-accelerated calculations during model training (CuPy, CUDA, Numba).

Despite the single training epoch, our denoised data reduced the low-frequency content of the real-space noise while preserving key information. To verify the quality of the denoised datacube beyond visual inspection, we compared it with the original datacube. We calculated the mean Peak Signal-to-Noise Ratio (PSNR) and Structural Similarity Index (SSIM), using the global maximum intensity and the global data range of the original datacube. The denoised datacube achieved a mean PSNR of 36.86 ± 0.71 and a mean SSIM of 0.8695 ± 0.0007, compared to 31.68 ± 0.19 and 0.8382 ± 0.0077 of the noisy datacube.



Though the training required several hours on a high-performance computer, denoising an image with a trained model is a much less computationally-heavy process, which can, in principle, be adapted to live data streams such as the acquisition of 4D-STEM datacubes. In the final part of the project, we started building a simulation of such a data stream to adapt our denoising model to run in real time. This puts the project close to deployment for live denoising.

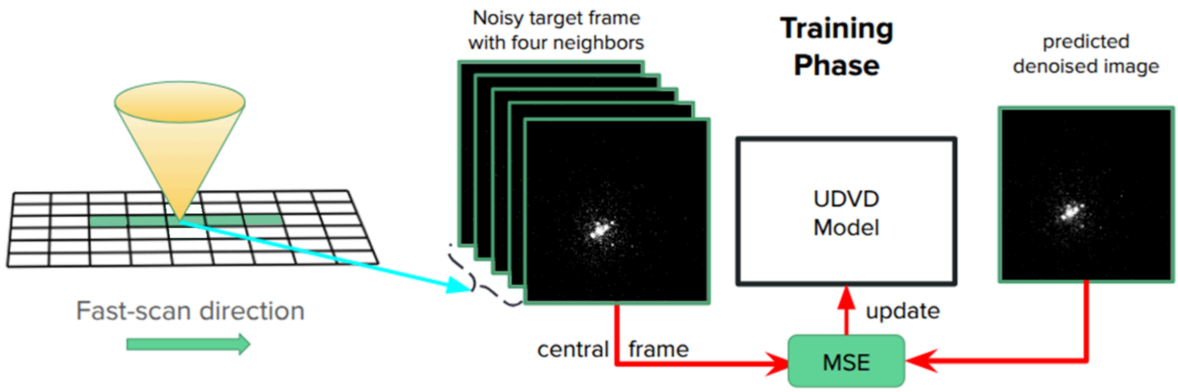


Fig:. Flowchart illustrating the data collection pipeline and unsupervised training of the deep denoising model (UDVD), enabling denoising of diffraction images at each scanning location without requiring ground-truth data.

Future work

We made steps towards inline denoising during data acquisition. We modified our method to operate on a sequence of 2D image files (one for each diffraction pattern), like those delivered by an imaging detector in 4DSTEM. We expect to complete this work and demonstrate live or near-live denoising of data during acquisition in the next few months.

References

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