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Physics-informed machine learning for microscopy

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Abstract. We developed a physics-informed deep neural network architecture able to achieve signal to noise ratio improvements starting from low exposure noisy data. Our model is based on the nature of the photon detection process characterized by a Poisson probability distribution which we included in the training loss function. Our approach surpasses previous algorithms performance for microscopy data, moreover, the generality of the physical concepts employed here, makes it readily exportable to any imaging context.

In any optical and non-optical imaging technologies, measurement comes with a noise addition producing a signal that follows a Poisson probability distribution (PPD). Signal enhancement algorithms increase the amount of information by increasing the signal to noise ratio (SNR), making them useful for modeling and visualization of biological data including: microscopy images representing light; medical imaging; computer tomography; positron emission tomography and other in-vivo imaging technologies.

Deep neural networks (DNNs) [1–7] based algorithms achieve the best results in signal enhancement. The performance and the ability to train DNNs, however, depends both on the chosen loss function – a quantity comparing predictions and target that DNN minimizes to learn its internal parameter – but also on the normalization of the network inputs and targets8. The simplest and more frequently used loss functions for denoising, but also in other image enhancement tasks is either the L1-norm or the L2-norm (MSE) [2,4,9,10], where the data are arbitrary normalized. On the other hand, when the desired output comes from a known probability distribution like in semantic segmentation (U-net[11]), or other classification tasks, an entropic loss function, and a probabilistic normalization of data, is of great significance. Although accounting the physics of the camera detection process is known to significantly improve imaging efficiency [12], little research has been done in applying this physical properties in DNNs.

Physics-informed machine learning is a new trend in artificial intelligent [13] and encoding the physics and statistics of light in a DNN is a missing puzzle. Here we report about physically informed DNN which builds on the PPD of signal detections. Our approach aims to provide a general and exportable approach to deal with PPD signal detection: I) we use a non-arbitrary and physics-based normalization process, II) we employ a physically informed loss function, and III) we design DNN architecture which works coherently with the approach. First, we remove any arbitrariness on the normalization just working with images in which each pixel count represents the photon number. Then we design a loss function which considers distance between probability distributions instead of the distance between count number. This enables the algorithm to work with the same efficiency in all dynamic range windows. We employ a custom DNN architecture capable of classifying each pixel on a predicted photon number, thus preserving the photon number encoding and meaning for the output images. We further show that the advantages of the semantic segmentation of U-net and the denoising power of RCAN can be combined in a unique architecture, we call it RESUNET.

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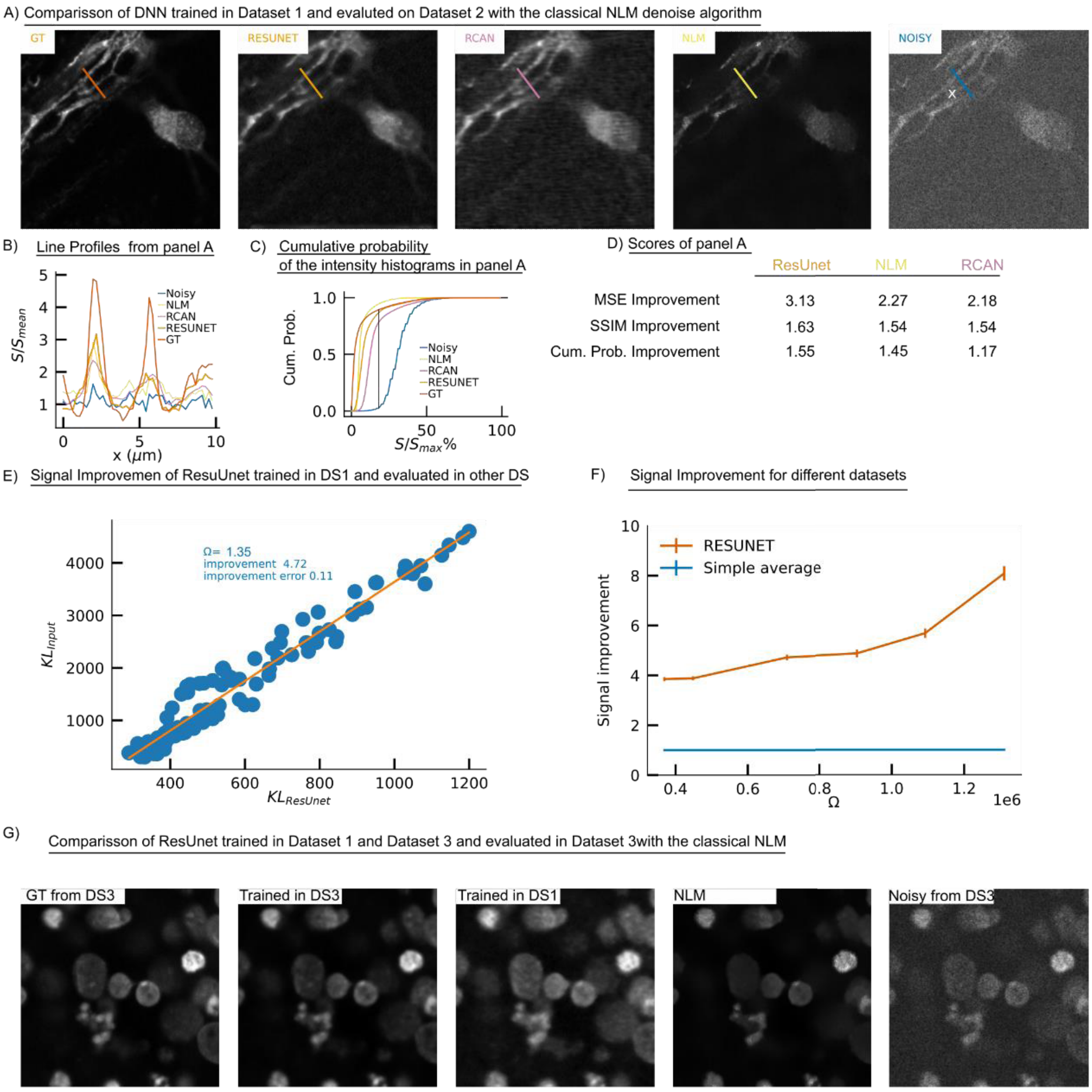

Figure: A) The comparison of the ResUnet with RCAN and NLM algorithm reconstruction of a Noisy input 10msec exposure (Noisy) for a Noci cell image slice from Dataset 2 with the corresponding GT (500msec exposure). Both ResUnet and RCAN have been trained in a different dataset 1. Characterized by different optical systems, fluorophores, and cameras. B) the line profile of the panel A for the line shown above C) The Cumulative probably of the intensity which is characterized by the Kolmogorov distance (vertical line) for panel A. D) The MSE, SSIM, Cumulative probability improvements for Panel A. E) We define the signal Improvement as the slope between the KLinput and the KLResUnet scatter plot linear fit. which we find for each different dataset here shown just for one characterized by the parameter F) The Signal improvements for different datasets with different $\Omega = \frac{V_{input}}{V_{psf}}$. G) Comparison of ResUnet for the same DS trained and different and comparison with the NLM.