Self-Supervised Learning for Single-Molecule Localization Microscopy Denoising

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Abstract

We will evaluate the ability of self-supervised Poisson denoising on SMLM. Single-Molecule Localization Microscopy (SMLM) images are predominantly corrupted with Poisson noise. There are currently existing methods for producing super-resolved SMLM images. There is a need for more accurate SMLM images in order for scientists gain a better understanding of the functions of live cells. By denoising SMLM images prior to super-resolution, we are hoping to increase the accuracy of the super-resolved SMLM image, thus allowing more exact molecule locations to be determined. We can denoise SMLM images utilizing only the original noisy images as training data with a Self-Supervised Deep Learning model. By modifying the previous Self-Supervised techniques that have been successful in denoising images with Gaussian noise, we will remove Poisson noise from SMLM images.

Introduction

For SMLM data to be of more use for understanding the cell function at the molecule level, the images need to pin point the exact location of individual molecules. Due to the nature of SMLM images, only a single noisy instance of a signal is available for a given instance of an image. Without a clean version of an image's signal, the use of a traditional deep learning approach that trains by mapping noisy images to the corresponding clean ones is not possible.

The current state-of-the-art super-resolution techniques which utilize deep networks include DeepSTORM, a CNN that trains on simulated and experimental data, and certain General Adversarial Networks which look to estimate the finer details and textures found in images. (Nehme et al. 2018; Ledig et al. 2017). These methods are not in use or practical options for SMLM, rather more traditional super-resolution remains common practice for the super-resolution in SMLM.

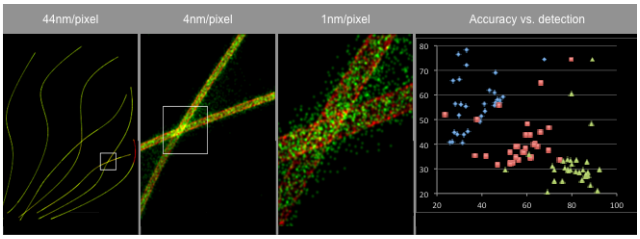

Figure 1: Results of SMLM super-resolution using traditional resolution techniques. (bio)

Traditionally, for the best preformance deep learning approaches to image restoration and the denoising of corrupted images has been done using a supervised deep network that utilizes pairs of corresponding corrupt and clean images. Specifically, there are content-aware image restoration (CARE) networks that have proven useful for denoising fluorescence microscopy data given noisy and clean images (Weigert et al. 2018). Techniques such as these are rendered useless when considering SMLM data which has no way of obtaining clean images.

Related Work

New findings have shown that despite the limitations of solely individual noisy SMLM images, denoising to the preformance level of supervised deep networks could be possible. The work of Lehtinen et al. shows that it is no longer necessary to provide a clean instance of an image (2018). In NOISE2NOISE (N2N), they show by training using pairs of two corresponding noisy images that share the same signal they are able to achieve as good, if not better (when training with finite data) performance for denoising. This method still requires at least 2 noisy realizations of a images signal.

Building off the ideas from N2N, worked called NOISE2VOID (N2V) shows that you can build a model for denoising using only individual noisy images for training data (Self-Supervised) (Krull, Buchholz, and Jug 2018). N2V introduces the use of a blind-spot network which masks a pixels data from the network's receptive field and allows the data surrounding said blind-spot to effectively predict the the pixel's signal. The N2V model is limited because it assumes every pixel's signal is dependent of the signals surrounding it.

To address the limitation of N2V, Laine et al. designs a different blind-spot architecture that by using 4 different receptive fields allowing more pixels to contribute to the loss function while maintaining the blind-spot (2019). In order to predict the blind-spot pixel's signal they apply a MAP desnoising procedure during testing that allows for the prediction of the clean signal to take into account the masked pixel. This is method can preform on par with

the supervised tradional deep denoising models under the assumption of Gaussian noise in the data.

More continued work since N2V is also attempts to predict the blind-spot pixel without the Gaussian noise model prediction (Krull, Vicar, and Jub 2019). PROBABILISTICNOISE2VOID (PN2V) model trains a probability distribution for 800 possible output values for a given pixel. PN2V is able to out preform N2V using the same U-Net architecture, but does not preform to the level of traditional supervised techniques.

Research Questions

1. How well can self-supervised learning denoise SMLM images?
2. Does denoising SMLM images prior to super-resolution improve the ability to locate and learn from the images?

Method

By utilizing the blind-spot architecture designed by Laine et al. while also implementing an adjusted method for training the model and predicting the blind-spot signals output, we will be able to remove noise from SMLM images. In the process described by Laine et al. Poisson noise is approximated by considering a Gaussian distribution with $\sigma^2 = \lambda$ (2019). This estimate will only provide a strong approximation when the standard deviation within the Poisson noise is small.

To better train our network and more accurately estimate a masked pixel's signal while considering the Poisson noise present in SMLM, we need a process that can model the Poisson noise while producing non-discrete clean signal values. To do this we will introduce the conjugate prior for the Poisson Distribution, the Gamma distribution. If we represent the distribution of possible clean image signals by the Gamma distribution, our loss function can be easily calculated and our clean estimation of the masked pixel will be representative of the surrounding pixel values represented by their corresponding Poisson noise as well as masked pixel's noisy value.

Timeline

1. Week 2: Finalize proposal and choose data sets to evaluate on. Figure out our specific method to evaluate denoising capabilities based on background SNR.
2. Week 3: Add to the blind-spot network code to include Poisson/Gamma denoising techniques for loss function and MAP denoising.
3. Weeks 4-7: Begin implementing denoising of SMLM and evaluating progress.
4. Weeks 6-9: Apply current super-resolution method to denoised images and evaluate performance. (Both Quantitatively and Qualitatively)
5. Weeks 9 and 10: Finalize evaluations and write final paper.

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