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Deep Learning for Single Molecule Localization Microscopy

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Summary

Single Molecule Localization Microscopy (SMLM) enables researchers to interrogate nanoscale spatial details in a range of systems. Biological investigations benefit greatly from SMLM due to its ability to quantitatively investigate details of great importance such as protein distribution in the cell membrane or protein-protein interactions(Baddeley & Bewersdorf, 2018). However, SMLM set-ups can be quite expensive, imaging times can be lengthy and data analysis can require expert knowledge. Recently, Deep Learning (DL) algorithms have been developed to reduce imaging time and automate data analysis. Naturally each subsequent model aims to address a different shortcoming of the prior work and so there is a family of model architectures. However, there is not a singular location for researchers to have access to these models dedicated to SMLM. We developed the Deep Learning for Single Molecule Localization Microscopy (DL4SMLM) in Python using the PyTorch framework to democratize access to these models and lower the barrier of entry to SMLM.

Statement of Need

DL4SMLM is a Python package that uses the Pytorch DL framework to implement Convolutional Neural Nets (CNN) dedicated to SMLM. We created it for researchers and engineers who wish to use DL for SMLM in whichever field they practice granted they have sufficient data. Currently, there are six models:Super Resolution Convolutional Neural Network (SRCNN)(Dong et al., 2015), Deep-Stochastic Optical Reconstruction Microscopy (Deep-STORM)(Nehme et al., 2018), Skip-STORM, Unet for STORM (U-STORM)(W. Yao et al., 2018), Deep Residual STORM (DRL-STORM)(B. Yao et al., 2020), and Fast Dense Image Reconstruction based Deep Learning STORM (FID-STORM)(Zhou et al., 2023). SRCNN and Skip-STORM are novel architectures to the SMLM field. While SRCNN has been applied to perform the super resolution task in more traditional image processing tasks, its utility in SMLM is unknown. Skip-STORM's architecture is similar to Deep-STORM but a skip connection between the initial image and final layer is introduced to enable it to have a spatial context during its reconstruction phase which could assist it in emitter dense images. U-STORM is inspired by U-Net and adopts a similar biphasic architecture where in the first half the initial image is max pooled while simultaneously increasing channel number and the second half involves the up sampling and reduction in channel. It also contains skip connections that connect the features of the first half to the those of second half during image reconstruction. These models are implemented using the object-oriented programming paradigm enabling researchers to instantiate multiple models for a single data set to allow downstream comparison of inference performance. Additionally, we have implemented the L1L2 Loss metric first introduced in (Nehme et al., 2018) and used for all subsequent architectures implemented in this library. Other features include functions that automate the Training and Validation process for a user-set number of epochs in addition to a function that automates the inference procedure of a trained model on a test data set and reports the Structured Similarity Index Measure (SSIM) and the Normalized Mean Square Error (NMSE). To assist researchers in visualizing the emitter localization performance of their model, we have implemented a function that visualizes the diffraction limited image of the emitters, its super-resolved version, and the predicted super-resolved image according to the trained model. This empowers the researcher to troubleshoot the performance of the model and determine if the model should be retrained with different parameters or to proceed with the experiment. To faciliate the development of powerful yet accurate models we have implemented two functions that enable knowledge distillation between a teacher model and a student model: Hint Learning and Knowledge Transfer. Hint training automates the learning process of a student network to have its intermediate representation mirror that of a teacher network. Knowledge Transfer uses the attentive imitation loss function from (Saputra et al., 2019), the teacher model, and the ground truth data set to optimize the student network. Altogether, we aim for this package to serve as a widely used resource for any experimenter in the SMLM field.

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