## Project proposal - EE368 Digital Image Processing Sparse Recovery for 3D Localization Microscopy

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## 1 Project description

Localization-based super-resolution microscopy such as STORM and (F)PALM has advanced the resolution of optical microscopy up to tens of nanometers. Those techniques capture thousands of images and computationally locates sparsely-excited single molecules at sub-pixel level. The estimated locations are accumulated from the multiple images to reconstruct a single image achieving spatial resolution beyond optical diffraction limit. The algorithm was initially developed to estimate locations of completely-isolated emitters and was inherently not applicable for images with high molecular densities. This limitation increased the required number of images and restricted temporal resolution. To overcome this limitation, a method based on a sparsity promoting prior was applied to estimate the locations of single molecules whose emissions are spatially overlapping [1]. The method achieved 3 sec temporal resolution and performed live cell imaging. While some methods have already achieved accurate localization almost close to Cramér-Rao lower bound, there are trade-offs between accuracy and temporal resolution. Tens of algorithms have been developed for the localization based on different approach, and their performance has been quantitatively analyzed with a set of consistent criteria [2].

Even though most algorithms estimate the locations in 2D, several algorithms have been extended to estimate 3D locations from a single image by encoding axial information on a point spread function (PSF). For example, DH-PSF is designed to change its angle along optical axis so that the depth of an emitter can be estimated from the captured angle. While the 3D localization from low density images has been becoming matured, it is still challenging for high density images. Toward this difficulty, one initial attempt combined the dictionary-based sparse recovery with double-helix PSF (DH-PSF) [3]. Their method exploits a dictionary whose columns store 2D images of DH-PSFs shifted over a 3D super-resolution grid. Even though their method was shown to be effective for high density images, it incurs expensive computational cost to handle the huge dictionary so that an input image with more than  $100 \times 100$  pixels is impractical. Therefore, a large input image must be split into a number of small patches.

To overcome this limitation, we identify the image formation model of 3D single molecule localization microscopy with convolutional sparse model. Since our approach stores only a set of kernels with small support, a large input image can be used at a time. Furthermore, by exploiting a fast deconvolution algorithm for convolutional sparse model [4,5], we develop a computationally efficient algorithm for 3D localization.

## 2 Plan

This project involves image deconvolution, filtering, and discrete Fourier transform taught in EE368. We plan to implement an image capture simulator of sparsely-located emitters in three dimensional space and develop a sparse recovery algorithm for 3D-localization microscopy. The simulator and the algorithm will be implemented on MATLAB. The developed algorithm will be characterized based on the simulated images. We also plan to explore another way to improve robustness and localization accuracy of the estimation by following approaches introduced for sparse spike deconvolution [6].

## References

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