FAST SINGLE MOLECULE LOCALIZATION USING GRAPHICS PROCESSING UNITS

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***Abstract*—We demonstrate maximum likelihood estimations of fluorophore positions in 2D and 3D using algorithms optimized for or accelerated by graphical processing units. The result is a reduction in computation time by two orders of magnitude.**

Keywords-super-resolution; fluorescence;

I. INTRODUCTION

In the application of single molecule localization based super-resolution (SML-SR), each reconstructed image may require up to 10^6 position estimates. One way to make this analysis tractable is trade optimal position estimation for speed [1,2,3]. However, with sufficient computation power, this trade-off need not be made. Modern Graphics Processing Units (GPUs) are available that have nearly two orders of magnitude greater floating point processing power than their CPU equivalents. Here we show that performing positions estimates on GPU hardware allows use the use of the efficient maximum likelihood estimator and results in a reduction of computation time by up to two orders of magnitude as compared to CPU implementations. Here we discuss three algorithms implemented on GPU hardware (1) Single fluorophore fitting in two dimensions; (2) Multiple fluorophore fitting in two dimensions; and (3) Single fluorophore fitting in three dimensions using a dual focal plane setup and phase retrieved pupil functions.

II. GPU ALGORITHMS

A. Single Molecule Localiztion

Single molecule localization in two dimensions can be performed by on GPU architecture by taking advantage of the simple parallelization of simultaneously analyzing many small fitting sub-regions. However, due to the details of GPU hardware, all data must by processed by identical steps of computation. By using a 2D Gaussian approximation to the microscope point spread function and a Newton-Raphson iterative update method, we have shown that position estimations using the maximum likelihood estimator can be implemented on the GPU [3]. With inexpensive commodity GPUs, position estimations can be performed at rates up to 10^6 fits per second.

B. Simultaneious Multiple Particle Localization

SML-SR imaging techniques require repeated localization of many single fluorophores. If, during analysis, successful localization does not require isolated fluorophores, the performance can be improved in one or more of several metrics that result in higher single-frame density of active fluorophores. For example: Data acquisition time can be reduced; A larger number of fluorophores can be localized; There is a higher tolerance on labeling density; and Dyes with higher minimum duty cycle can be used.

We have developed a method that uses the maximum likelihood estimator to localize multiple fluorophores simultaneously within a fitting sub region [4]. We find that for a fitting region of size approximately 1 square micron, localization of up to 5 fluorophores provides a good compromise between fit accuracy and analysis time. The algorithm is implemented on the GPU architecture in a manner similar to our single molecule analysis and achieves near real-time analysis speed under many practical conditions.

We show the performance of multiple fluorophore fitting as a function of the maximum allowed number of fitted fluorophores and the single-frame active emitter density. We describe the details of the algorithm that allow robust fitting, the details of the GPU implementation, and the other imaging processing steps required for the analysis of SML-SR data sets.

C. Three Dimensionional Localzation using a Dual Focal Plane Setup and Phase Retrieved Pupil Functions.

Fluorophore position estimation in three dimensions often use simple Gaussian models, theoretical PSFs that do not account imaging system aberrations, or large, unwieldy, experimentally acquired 3D PSFs that can be prone to artifacts. Here we introduce a localization algorithm based on phase retrieved pupil functions and the maximum likelihood estimator. Pupil functions can contain information about specific aberrations present in the imaging system and can be used to calculate realistic 3D PSFs from a small set of Zernike polynomial coefficients that describe the pupil magnitude and phase [5]. This compact representation of the 3D PSF allows the PSF to be efficiently calculated as needed in an iterative update method implemented on GPU hardware in a similar fashion to our two dimensional localization algorithms. We

demonstrate the use of phase retrieved pupil functions for 3D localization in using a dual focal plane setup.

III. Conclusion

GPU hardware can greatly facilitate single molecule localization, allowing fast position estimation using the maximum likelihood estimators with both simple and complex imaging models.

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