COMPARING METRICS FOR INTENSITY-BASED ADAPTIVE OPTICS IN SINGLE-MOLECULE LOCALIZATION MICROSCOPY

M.E. Siemons, L.C. Kapitein
Department of Biology, Utrecht University
Padualaan 8, 3584 CH Utrecht
Email: m.e.siemons@uu.nl

KEY WORDS: Single-molecule localization microscopy, adaptive optics, deep tissue

Recent developments in excitation modalities and labeling strategies enable single-molecule localization microscopy in deep tissue (>20 um). However, sample-induced aberrations hamper optimal detection and localization, which can be overcome by intensity-based adaptive optics (AO). The need for fiducial markers or 'guide stars' in complex samples can be circumvented by using the single-molecule acquisitions themselves in combination with an appropriate metric, a measure for the quality of an acquisition. Here we compare the performance of different metrics suggested in literature [1-3] and a newly proposed metric by simulating single-molecule acquisitions in a wide variety of conditions using model-based optimization. This reveals that correction is challenging and that straightforward implementations do not guarantee improvement. We show that a series of 300 acquisitions with a combination of two metrics can robustly correct initial aberrations up to 1 rad rms below 0.3 rad rms (0.9 Strehl-ratio), restoring localization precision. The achieved aberration correction is experimentally verified on a DNA-PAINT sample by adding known aberrations that are subsequently corrected. These results reveal under which SNR conditions and aberration levels robust correction can be achieved.

[1] D. Burke, B. Patton, F. Huang, J. Bewersdorf, and M. J. Booth, "Adaptive optics correction of specimen-induced aberrations in single-molecule switching microscopy," Optica 2, 2015

[2] K. F Tehrani, J. Xu, Y. Zhang, P. Shen, and P. Kner, "Adaptive optics stochastic optical reconstruction microscopy (AO-STORM) using a genetic algorithm," Opt. Express 23, 2015

[3] M. J. Mlodzianoski, P. J. Cheng-Hathaway, S. M. Bemiller, T. J. McCray, S. Liu, D. A. Miller, B. T. Lamb, G.E. Landreth and F. Huang, "Active PSF shaping and adaptive optics enable volumetric localization microscopy through brain sections", Nature Methods, 15, 2018