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Wavelet-Based Spot Detection for Low Signal-to-Noise Ratios

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Abstract

- Spot detection algorithms play a critical role in scientific research.
- Low signal-to-noise ratio scenarios, such as single-molecule imaging, are particularly challenging.
- The algorithms I developed exhibit superior performance to the existing algorithms for a wide range of imaging conditions, including defocused point spread functions, non-uniform image backgrounds, and ranges of labeling density.
- For most imaging conditions, my algorithms do not require any parameter adjustment, avoiding tedious human intervention and potential subconscious bias.
- My algorithms are easily implemented and continue to enjoy the computational efficiency typical of wavelet-based spot detection.

Image Simulation

- Simulated images were generated for a range of biophysically relevant conditions

Signal

- Point sources were generated using the Born-Wolf point spread function (PSF)
- Monochromatic emitter at 655 nm, 100x magnification, numerical aperture 1.4, 16 µm pixel size
- Signal varied from 50 to 1000 photon counts per PSF

Noise

- Gaussian readout noise, mean of 1000 and standard deviation of 8 photon counts per pixel

Simulation Set 1

- Defocus varied from -500 to 500 nm defocus
- Well separated simulated PSFs

Simulation Set 2

- Additional Poisson-distributed noise to simulate varying background, varying frequency sinusoids with expected value

$$S(i,j) = 25\left(\sin\left(8\pi\left(\frac{i}{512}\right)^2\right) + \sin\left(10\pi\left(\frac{j}{512}\right)^2\right) + 2\right), i,j = 1,\ldots,512.$$

- Randomly distributed 3D locations, varying noise.
- Density of labeling varied from 80 to 1977 PSF's per 512x512 pixel image.

Algorithms

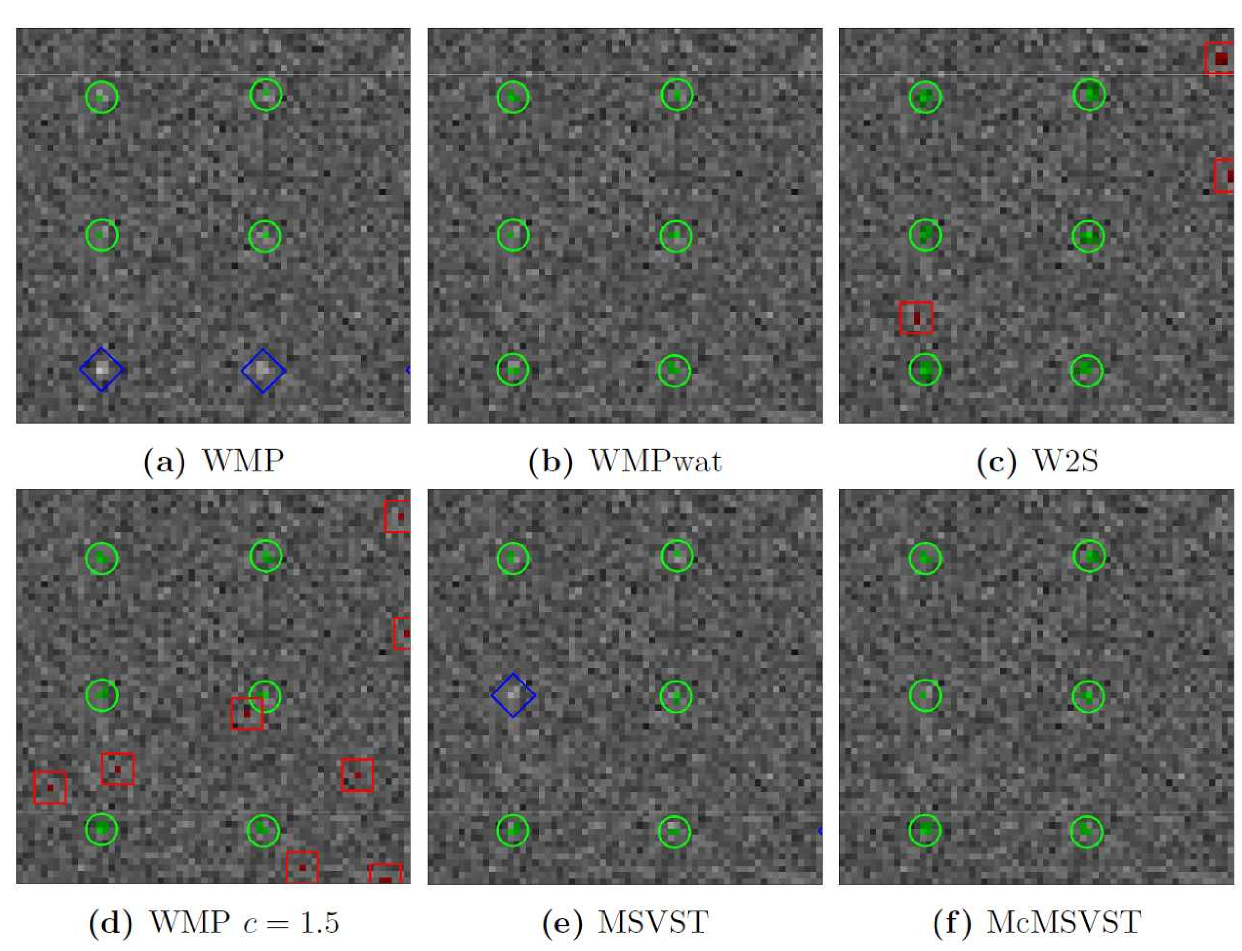
WMP – Wavelet Multiscale Product[1]
W2S – Wavelet 2nd Scale
MSVST – Multiscale Variance Stabilizing Transform[2]
WMPwat – New Algorithm
McMSVST – New Algorithm

Evaluation Criteria

Term	Definition
Spot	All detected pixels within two pixels of each other.
True Positive (TP)	Spots matching a simulated location.
False Positive (FP)	Detected spots which are not true positives.
False Negative (FN)	The number of simulated locations which should have been detected minus the number of true positive spots.
Sensitivity	$\frac{TP}{TP+FN}$, a measure of the fraction of spots detected that should have been, also known as recall, ideally 1.
Positive Predictive Value (PPV)	$\frac{TP}{TP+FP}$, the fraction of detected spots which are legitimate, also known as precision rate, ideally 1.

As we are interested in spot detection statistics, true positives and false positives are defined for spots rather than for simulated locations. A spot may match multiple simulated locations, but it will only register as a single true positive.

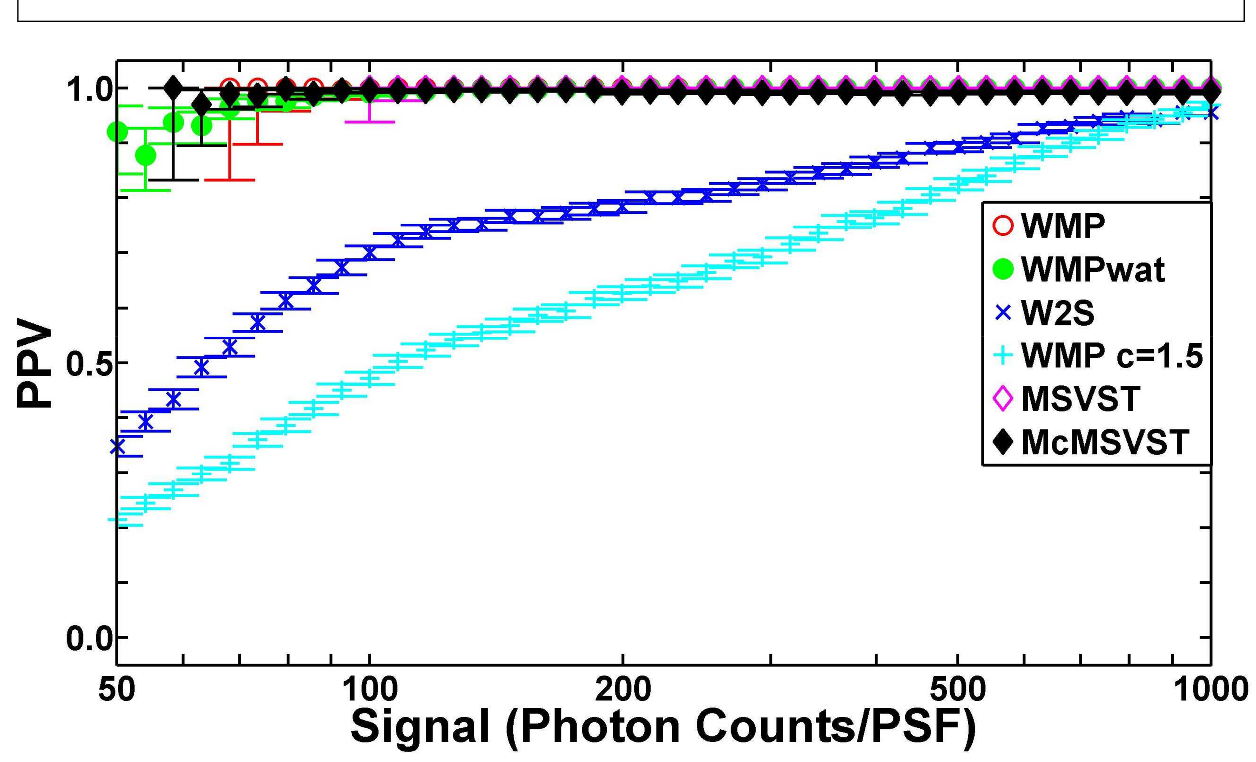
Simulated Data Set 1



(a) WMP (b) WMPwat (c) W2S
(d) WMP $c = 1.5$ (e) MSVST (f) McMSVST

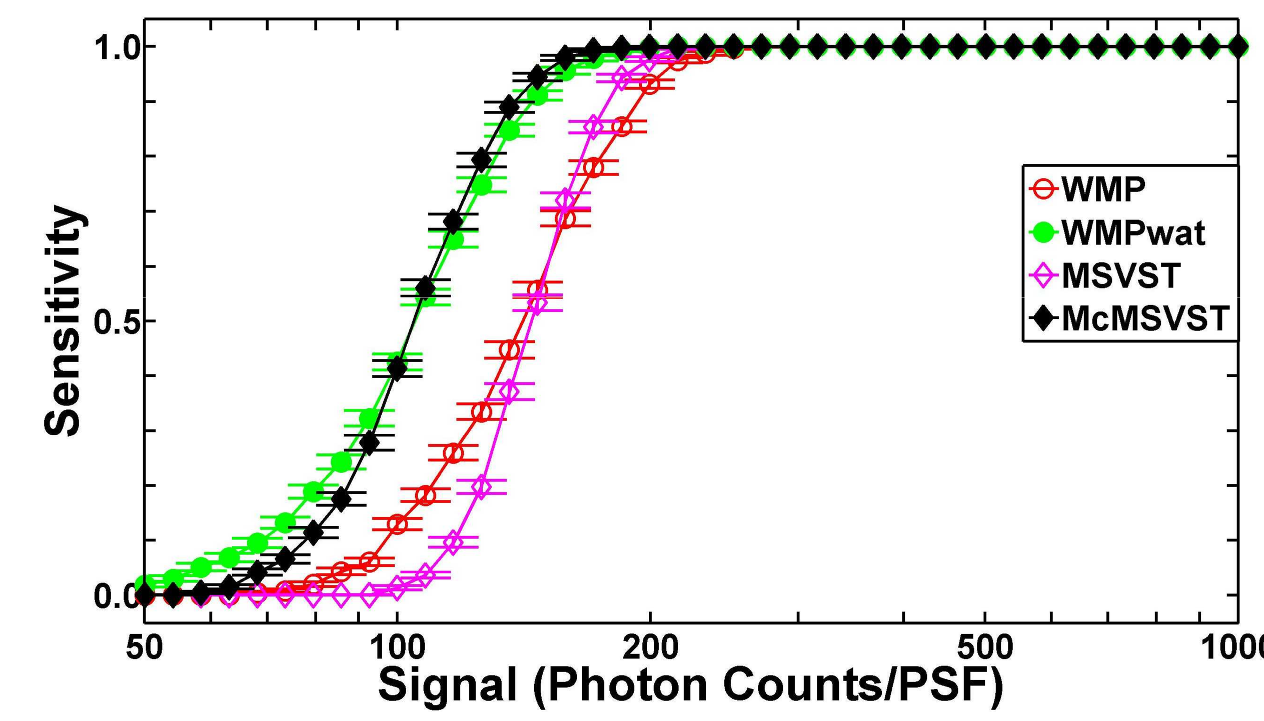
Comparison of the spot detection algorithms where sensitivity varies greatly. The spot detection results for a small portion of the images simulated with no defocus, 159 expected photon counts per PSF, and background standard deviation of 8 photon counts per pixel. True positives are circled in green, false positives are surrounded by red squares, and false negatives are surrounded by blue diamonds. The sensitivity of any algorithm can be improved by relaxing the control parameter, as seen by comparing (a) and (d) where the control parameter c has been reduced from 3 to 1.5. However, relaxing the control parameter also increases the number of false positives.

Constant Control Parameters



Ideally, algorithms can be run unsupervised, requiring no user interaction for a wide range of input images. **WMP with c=1.5 and W2S have insufficient PPV to be practical.**

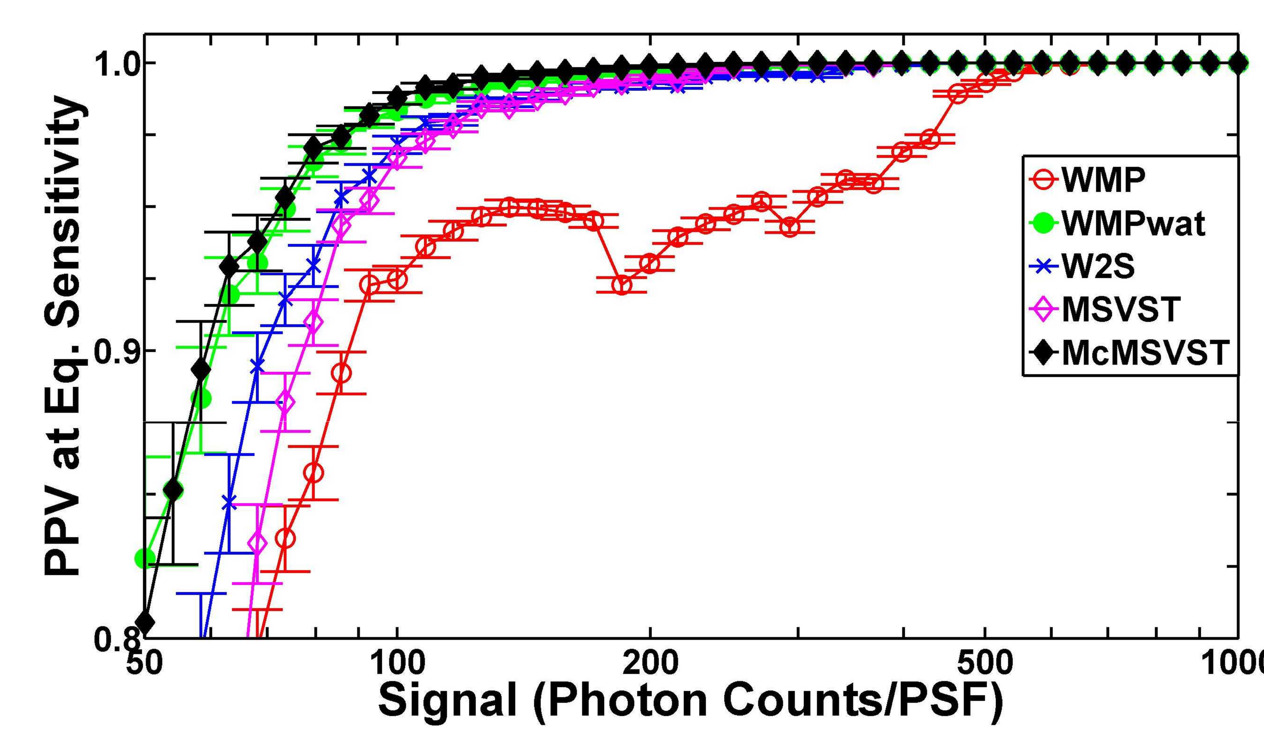
Constant Parameters (continued)



Of those algorithms which maintain high PPV, the new algorithms, **WMPwat and McMSVST, have higher sensitivity at low signal-to-noise.**

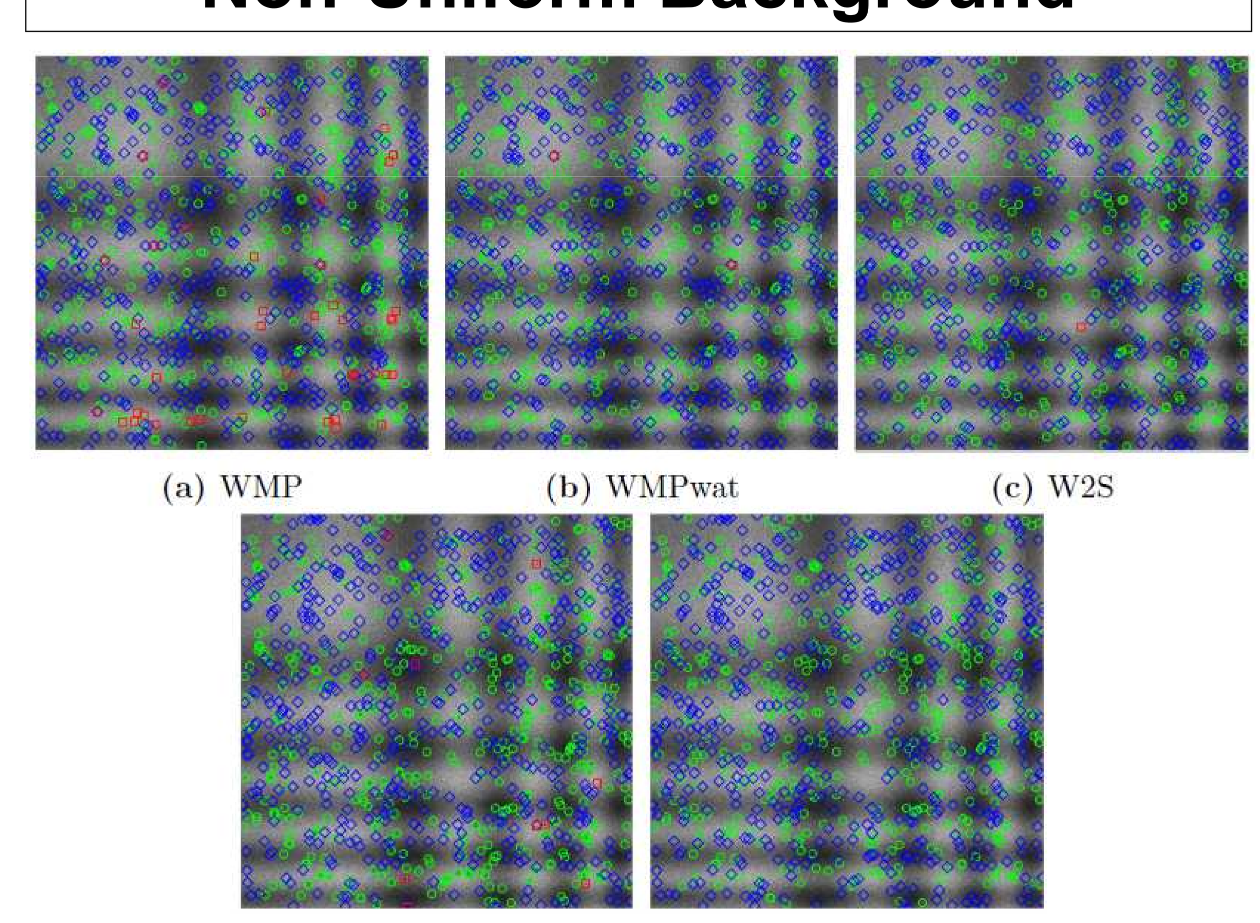
At Equal Sensitivity

As sensitivity can be increased at the expense of PPV by relaxing the control parameters, fair comparison requires adjusting the control parameters so that either sensitivity or PPV are equal.



At equal sensitivity, **the new algorithms perform the best**, with McMSVST slightly better than WMPwat.

Non-Uniform Background



(a) WMP (b) WMPwat (c) W2S
(d) MSVST (e) McMSVST

Comparison of the spot detect detection algorithms at equal sensitivity for a highly non-uniform background. The sensitivity is intentionally low to reveal the spatial distribution of false positives and false negatives.

References

1. Olivo-Marin JC (2002) Extraction of spots in biological images using multiscale products. Pattern Recognition 35: 1989-1996.
2. Zhang B, Fadili JM, Starck JL (2008) Wavelets, ridgelets, and curvelets for Poisson noise removal. IEEE Transactions on Image Processing 17: 1093-1108.