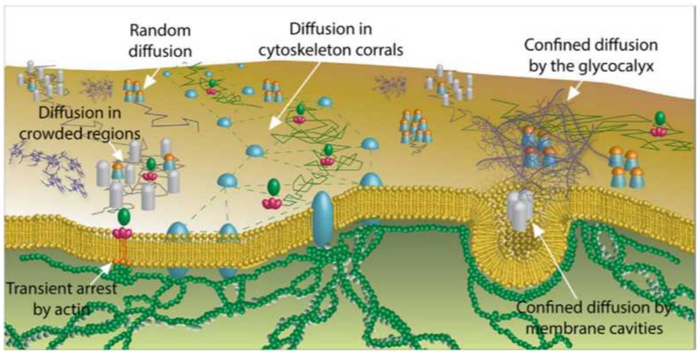
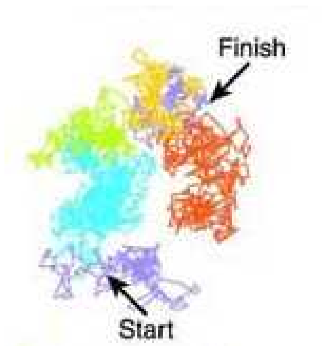
SAND2017-3612C





Detecting and Tracking Intermittently Observable Single Molecules

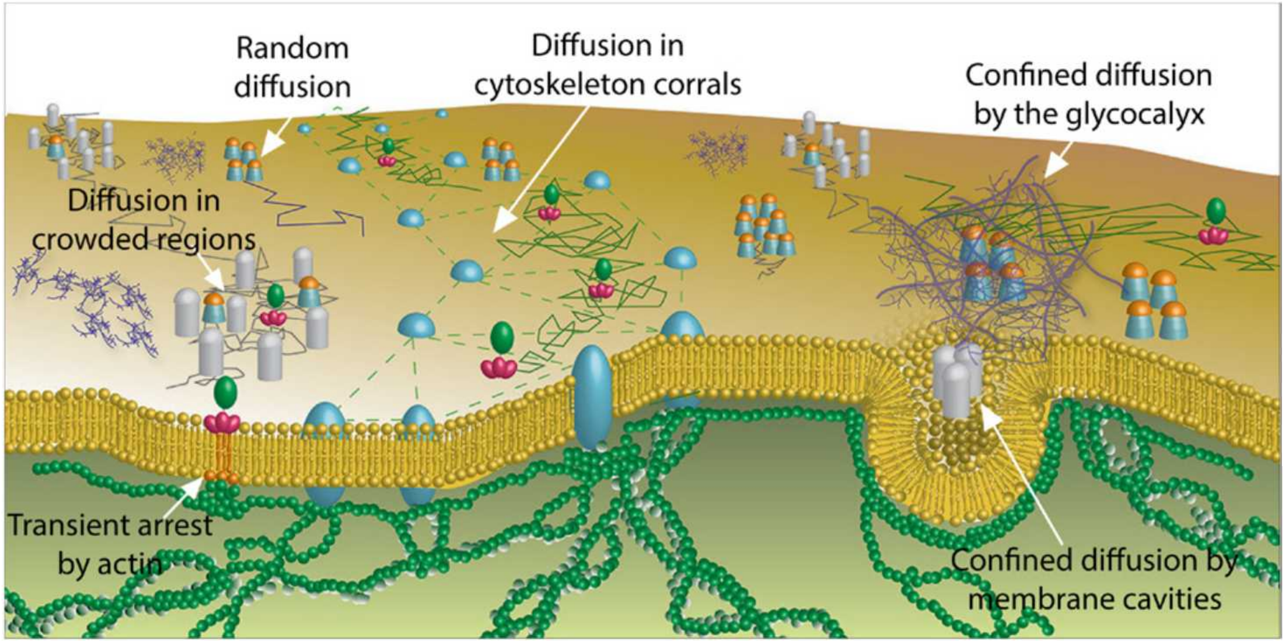
Stephen M. Anthony

Sandia National Laboratories is a multi-program laboratory managed and operated by Sandia Corporation, a wholly owned subsidiary of Lockheed Martin Corporation, for the U.S. Department of Energy's National Nuclear Security Administration under contract DE-AC04-94AL85000. SAND NO. 2011-XXXXP

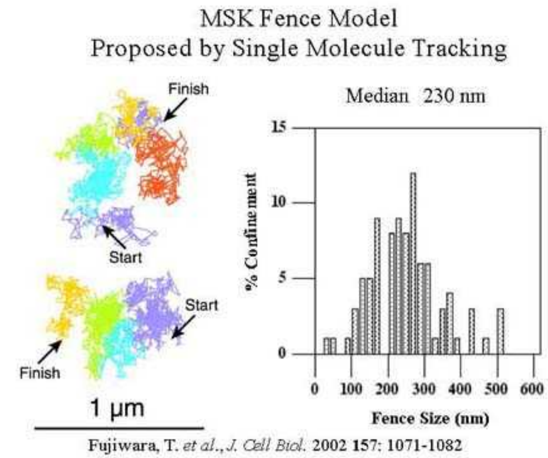
Outline

- Steps involved in single particle tracking (SPT)
- Wavelet based detection
  - Enhanced sensitivity at lower signal-to-noise ratios without an increase in false positives
- Graph theory tracking algorithm

Who Uses Single Particle Tracking?

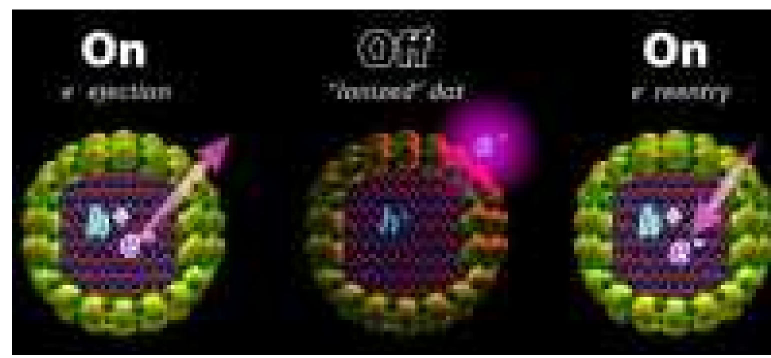


Manzo, C. and M. F. Garcia-Parajo (2015). Reports on Progress in Physics **78(12).**



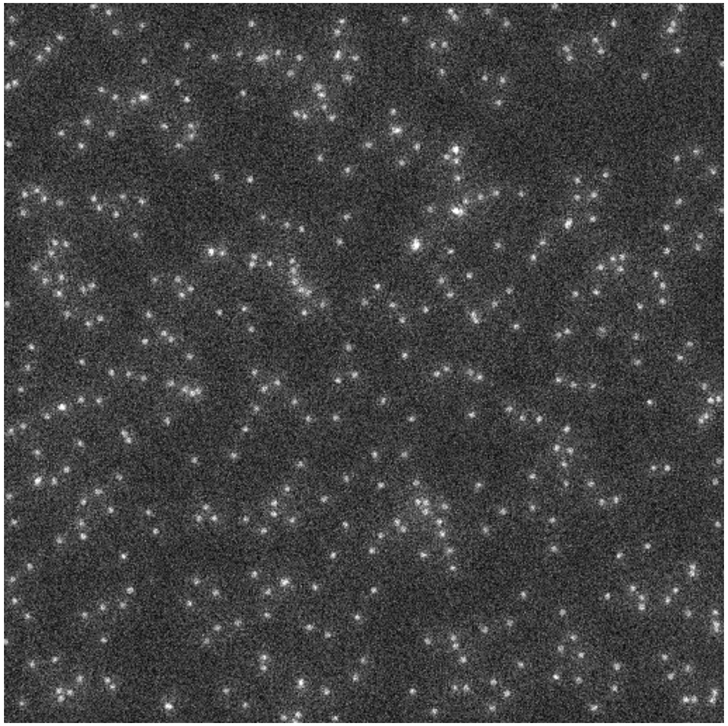
http://www.nanobio.frontier.kyoto-u.ac.jp/research/slide-show/slide04/#slide205

SPT is useful across many fields. However, single molecule biophysics present some of the most interesting and challenging problems. Not all particles can be detected in all frames!

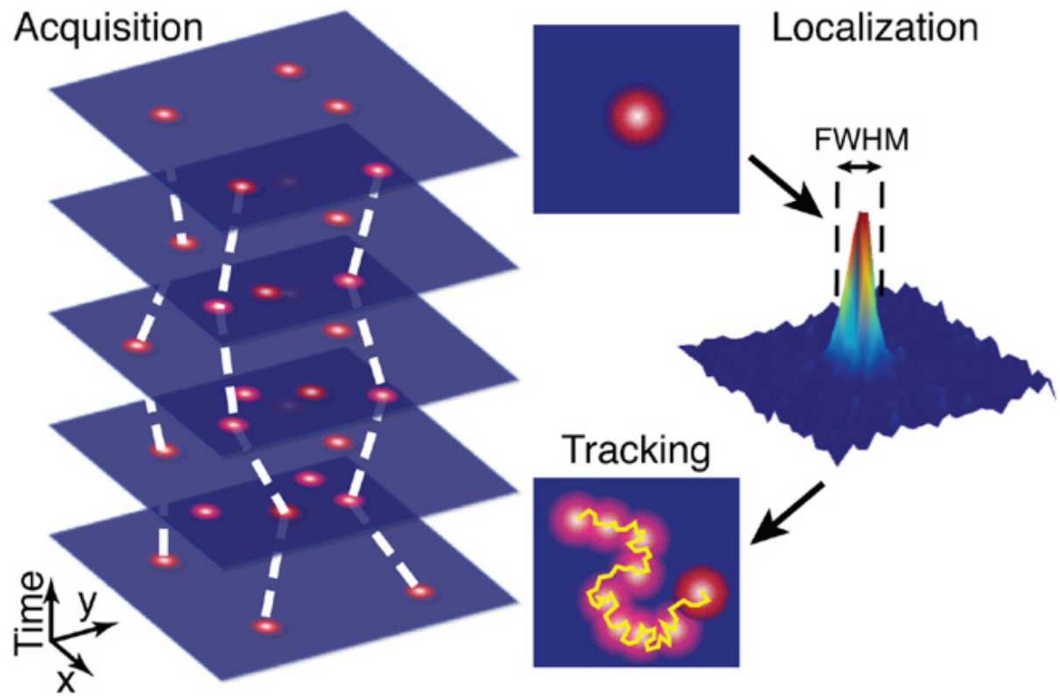


Credit David Nesbitt
https://jila.colorado.edu/research/nanoscience/nanostructures

Steps Involved in Single Particle Tracking



Chenouard, N., et al. (2014). Nat Meth **11(3): 281-289.**



Manzo, C. and M. F. Garcia-Parajo (2015). Reports on Progress in Physics **78(12).**

Single particle tracking process:

1) Detect – Separate signals from noise
2) Localize – Obtain sub-pixel or super-resolution coordinates
3) Track – Connect observations together

Outline

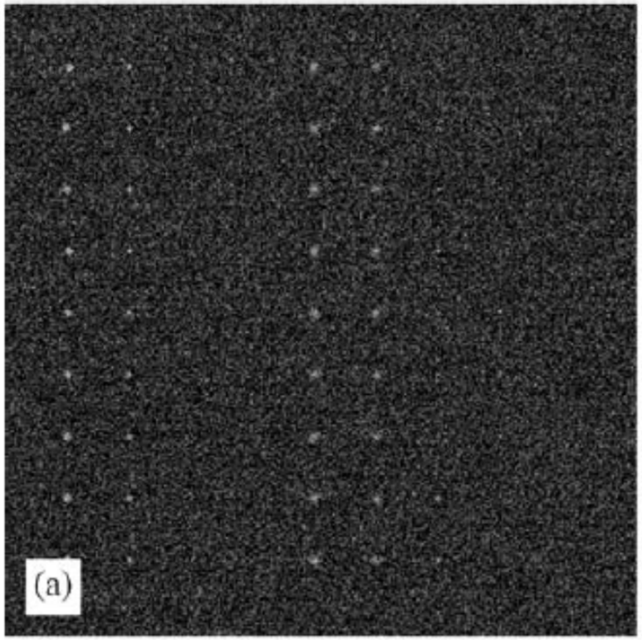
- Steps involved in single particle tracking (SPT)
- Wavelet based detection
  - Enhanced sensitivity at lower signal-to-noise ratios without an increase in false positives
- Graph theory tracking algorithm

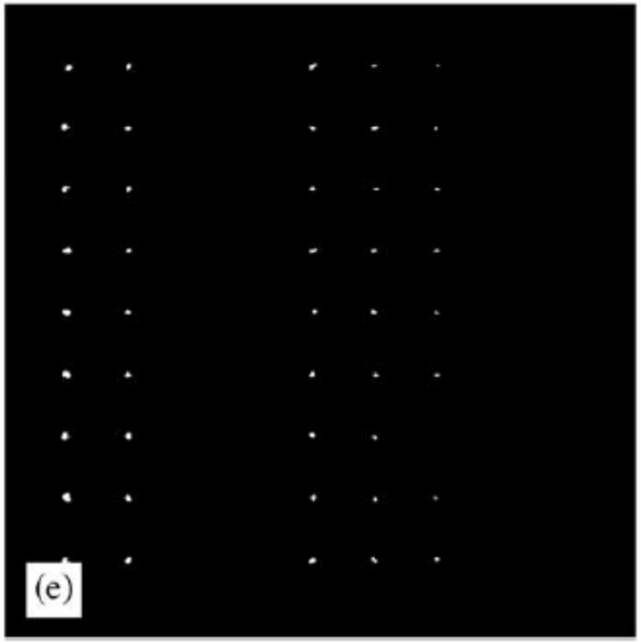
Wavelet based detection

Pattern Recognition 35 (2002) 1989–1996

Extraction of spots in biological images using multiscale products

Jean-Christophe Olivo-Marin*

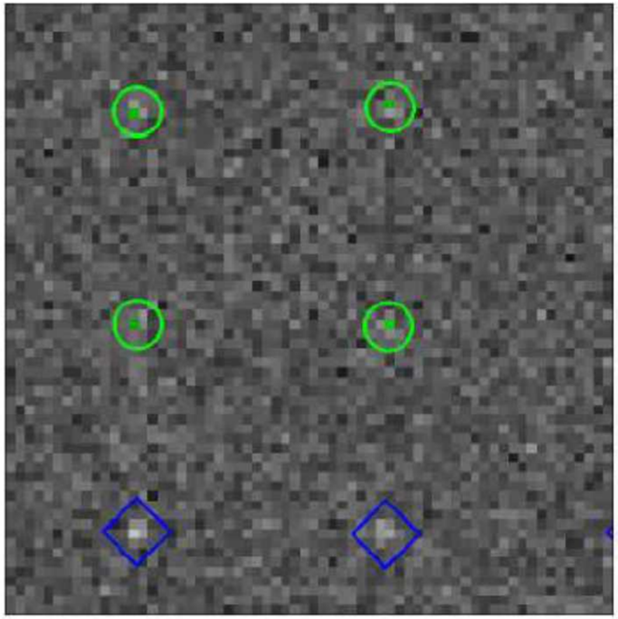




9 columns of simulated data, varying spot size

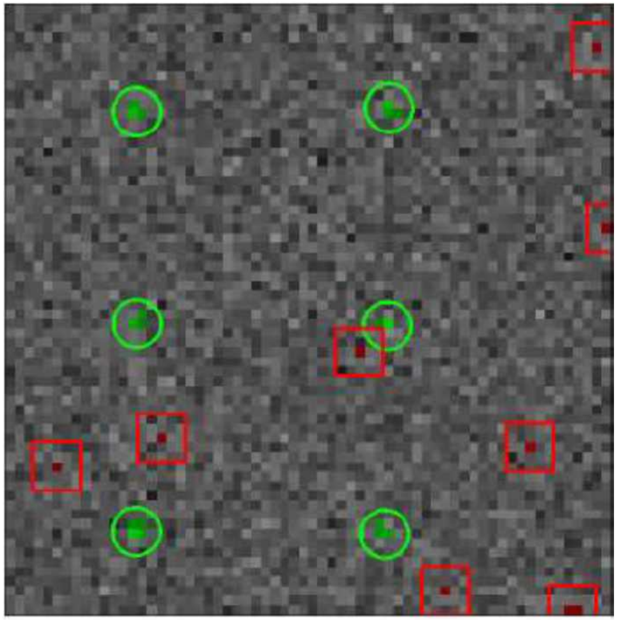
Reliable detection for certain conditions

Setting Parameters: Goldilocks Problem



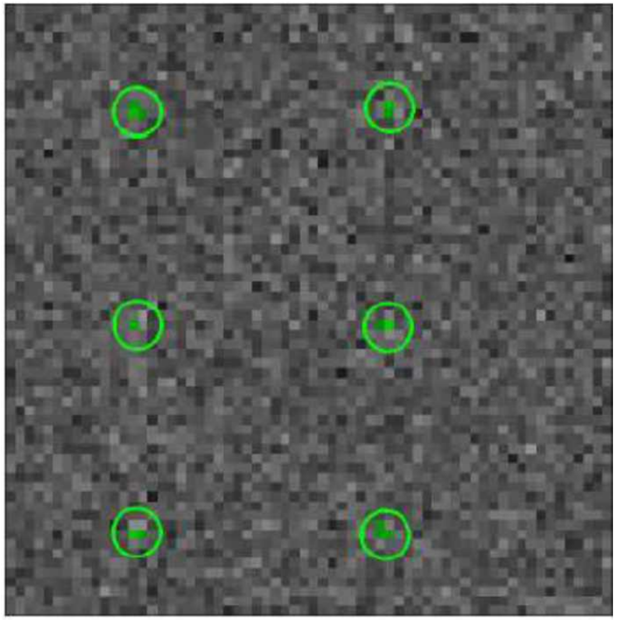
Too High

False Negatives



Too Low

False Positives

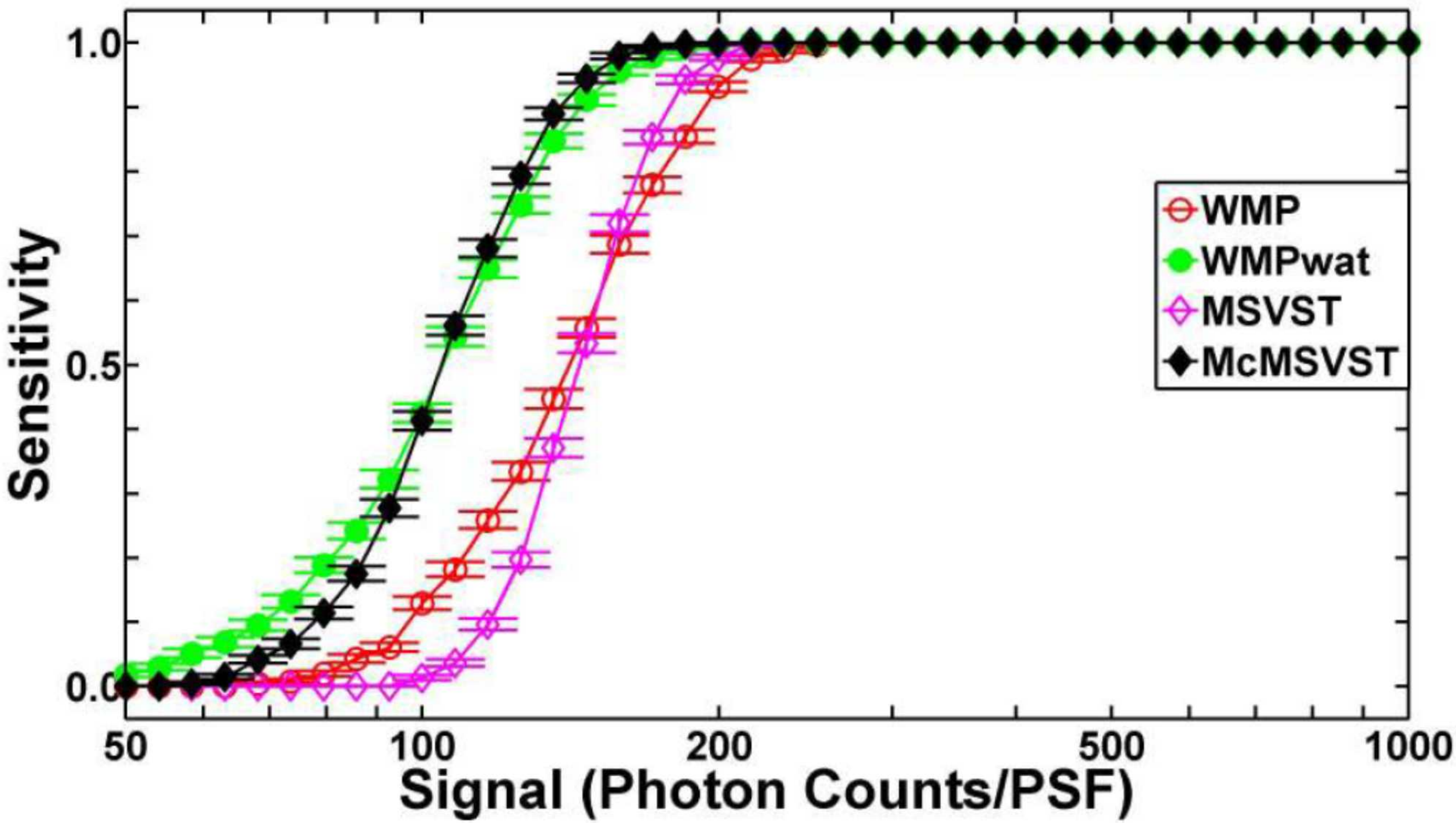


Just Right

True Positives

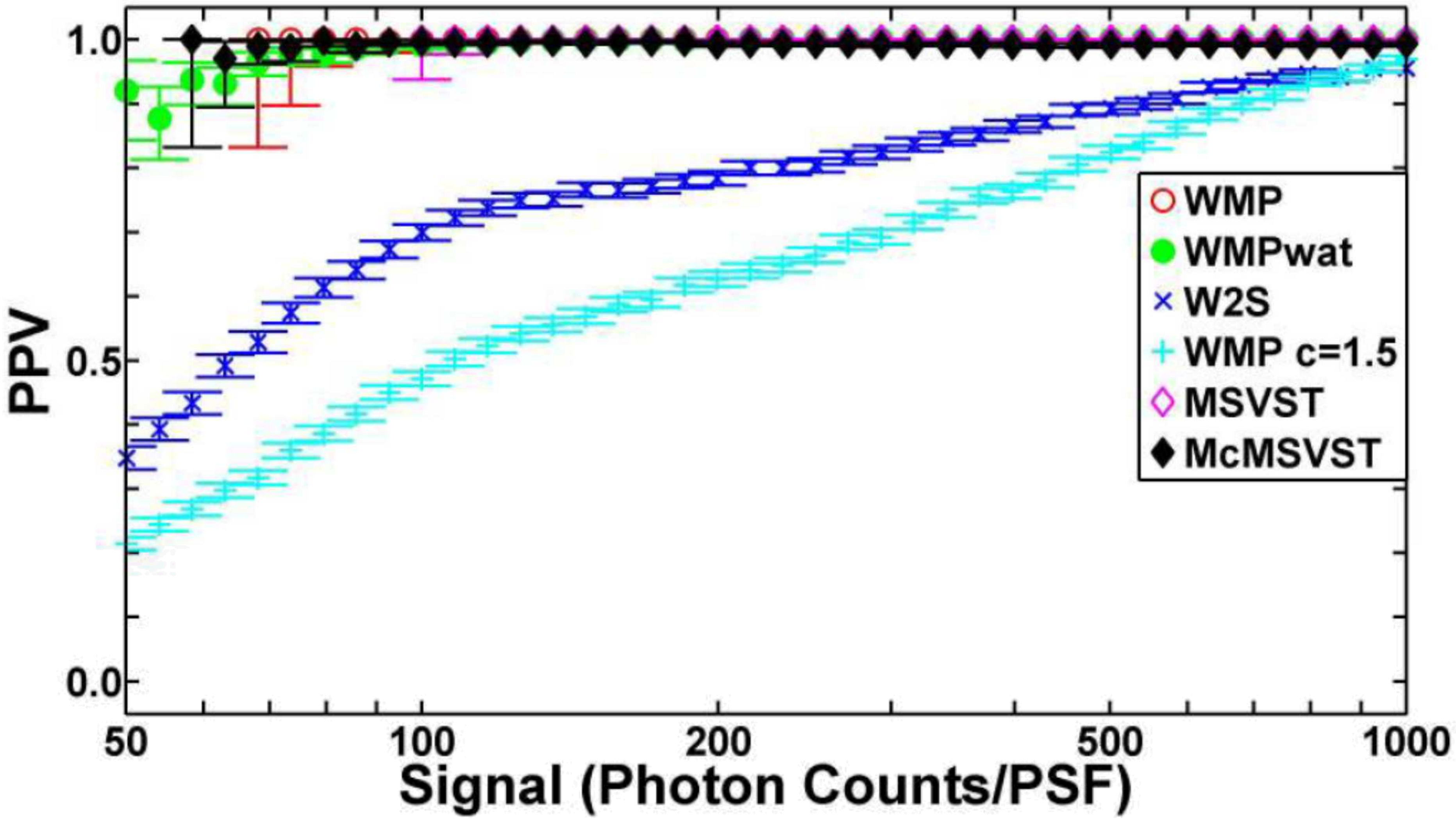
Olivo-Marin’s WMP algorithm has user adjustable parameters. The best value varies between images.

Adaptive Thresholding



Enhanced sensitivity at lower signal-to-noise ratios

Adaptive Thresholding



Without an increase in false positives

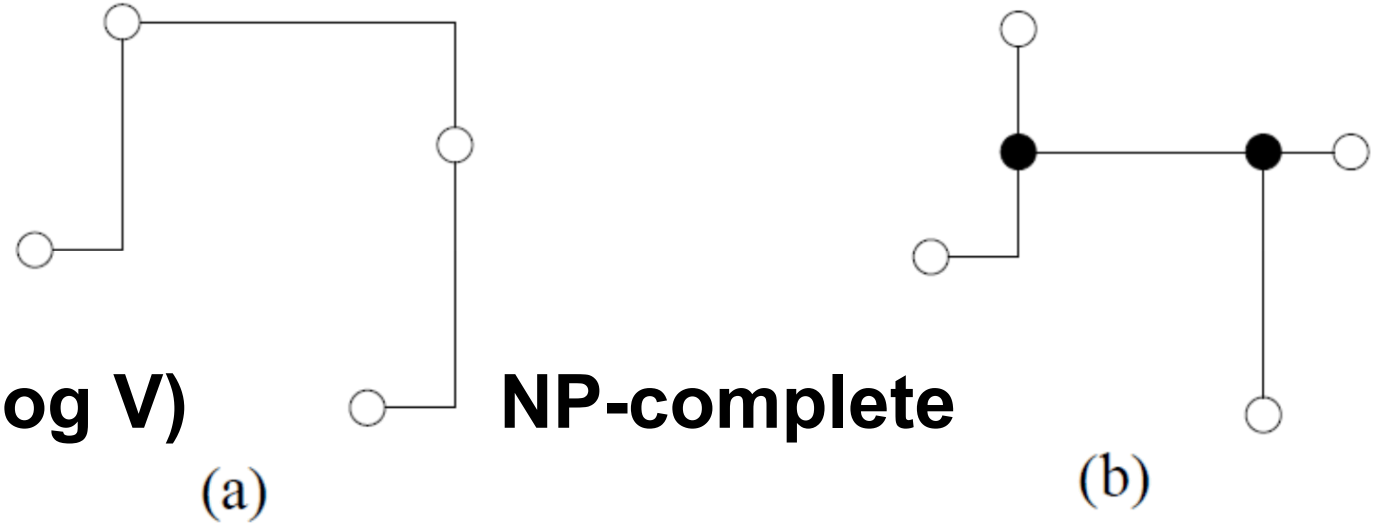
Outline

- Steps involved in single particle tracking (SPT)
- Wavelet based detection
  - Enhanced sensitivity at lower signal-to-noise ratios without an increase in false positives
- Graph theory tracking algorithm

Why is tracking a hard problem?

- Connecting observations between adjacent frames is an assignment problem – maximum bipartite matching.
  - A naïve algorithm would perform an O(V!) exhaustive search – impractical except for the smallest problems
  - Much more efficient algorithms, $O(V^3)$ or better, allowing large problems to be solved exactly in reasonable time
- Single particle tracking (SPT) is more complicated – not just a set of assignment problems
  - Assignment is not always 1 to 1 – can be one to many or many to one
  - Not every particle is seen at all times – **assignment must account for missing observations**
  - As a result, SPT is an NP-hard combinatorial optimization problem

Steiner Problem Analogy



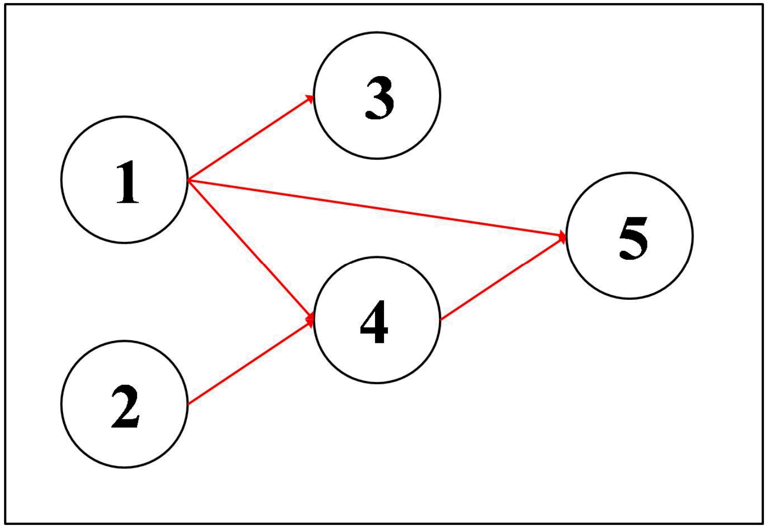
Gabriel Robins http://www.cs.virginia.edu/~robins/papers/Steiner_chapter.pdf

In the rectilinear plane, a) The minimum spanning tree (MST) and (b) the Steiner minimal tree (SMT). Hollow dots correspond to the points to be connected while solid dots represent Steiner points.

O(E log V)
Easily Solved

NP-Complete
Incredibly Hard

Framing SPT as an Adjacency Matrix



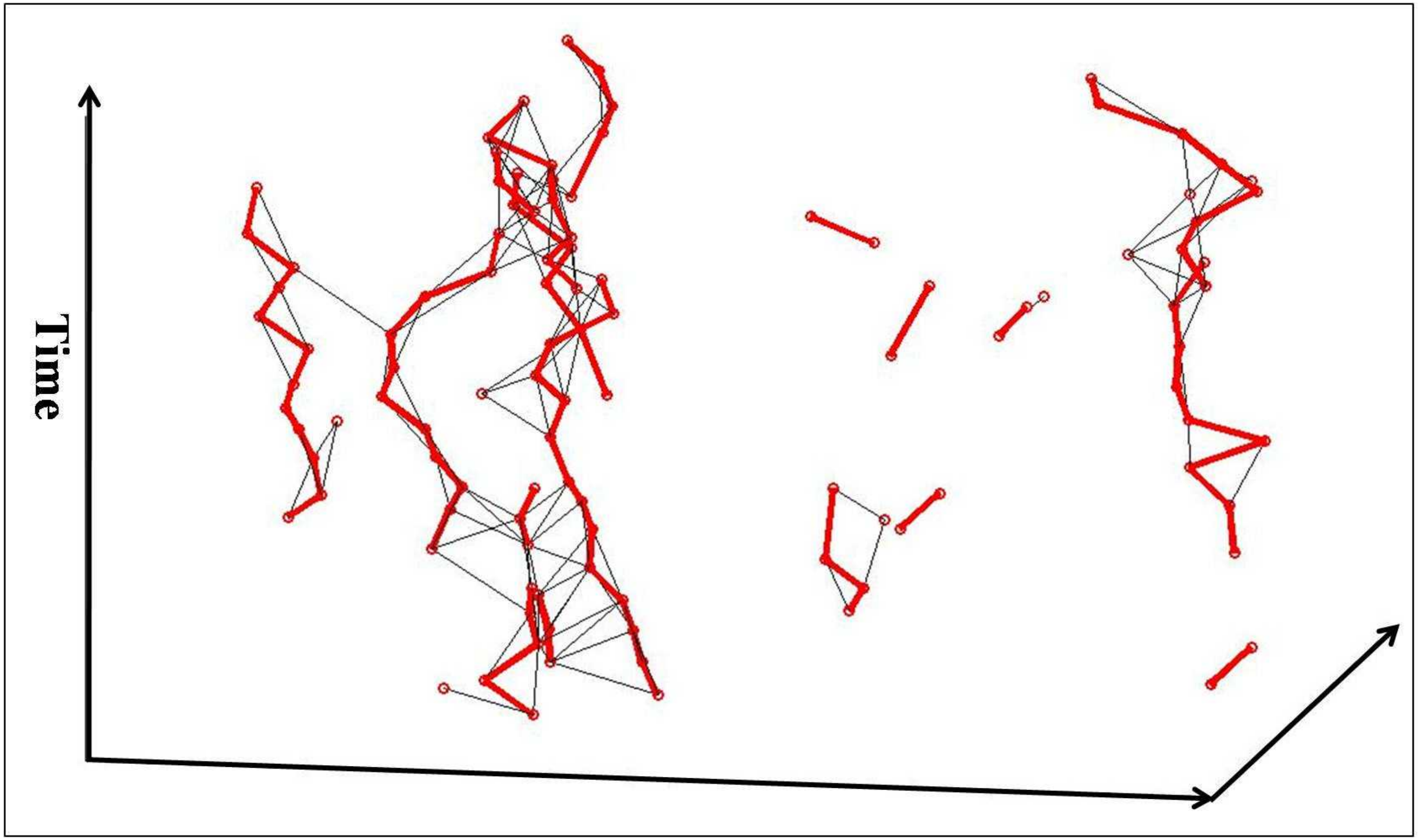
	1	2	3	4	5
1			1	1	1
2				1	
3					
4					1
5					

Sample Set of Observations

Corresponding Sparse Directed Adjacency Matrix

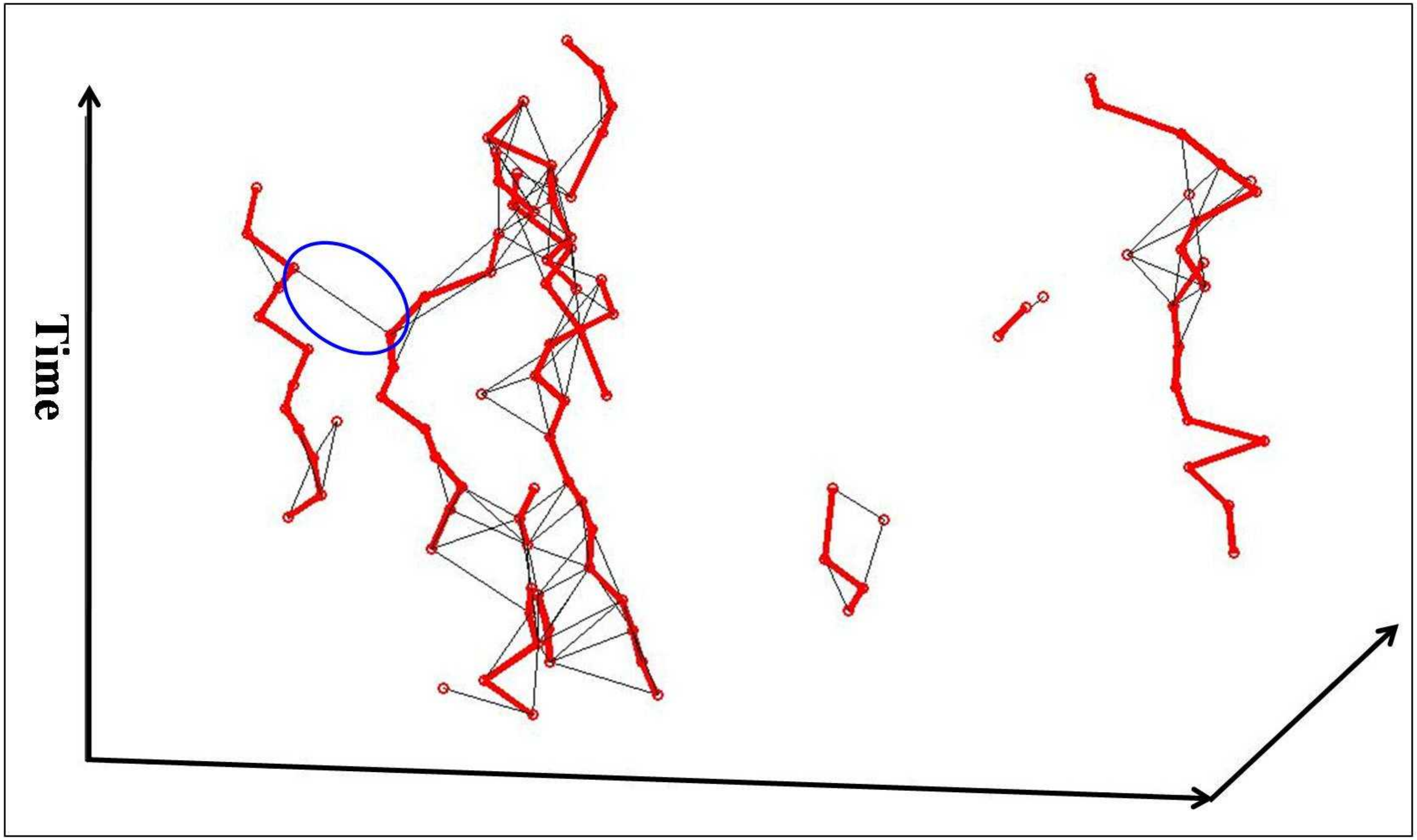
Simplified example – actual adjacency matrix would have
1) weights to represent the relative probability of the edges
2) twice as large. Expanded form allows accounting for missing particles and incorrect observations.

Removing Redundant Edges



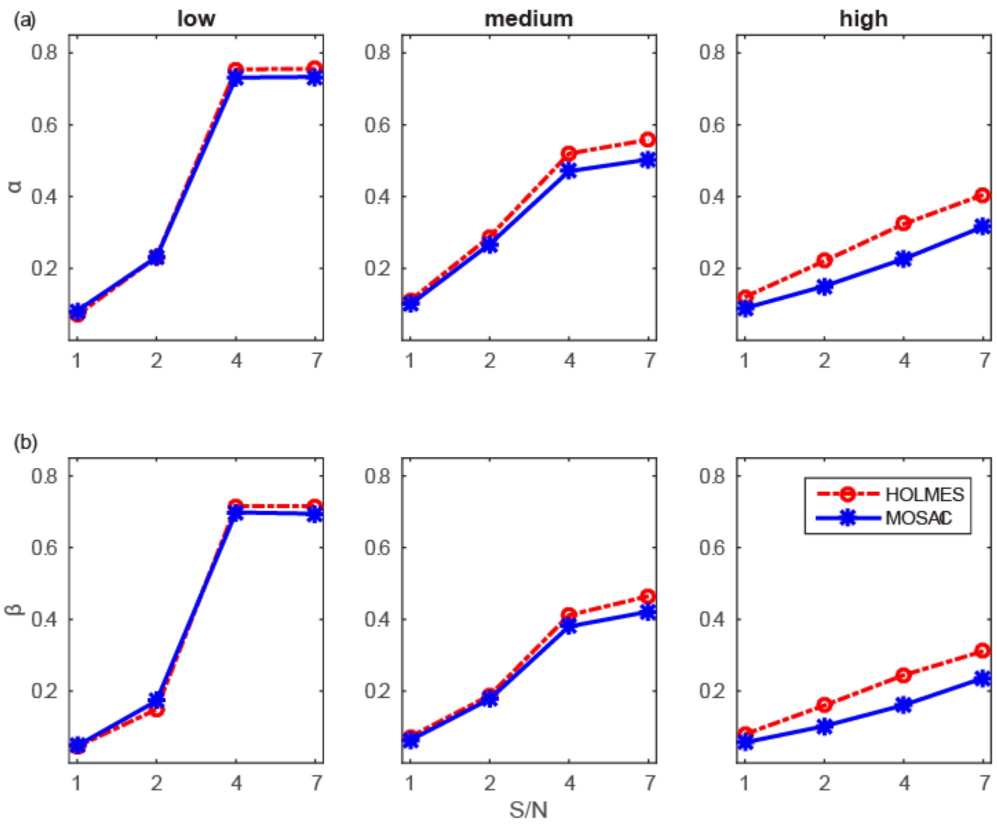
At this point, we have a directed acyclic graph, where any red lines correspond to shortest paths. Some edges are clearly redundant.

Pruning Redundant Edges



The redundant edges could not be part of the optimal solution. Removing them can greatly simplify the graph.

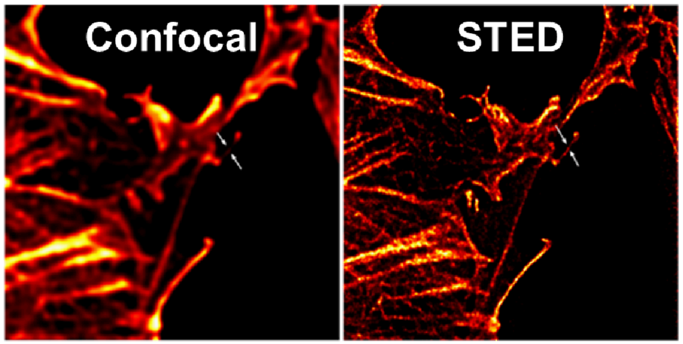
Performance



Comparison of our algorithm (HOLMES) to one of the best performing algorithms in the ISBI 2012 Particle Tracking Challenge on datasets from the challenge. Higher is better.

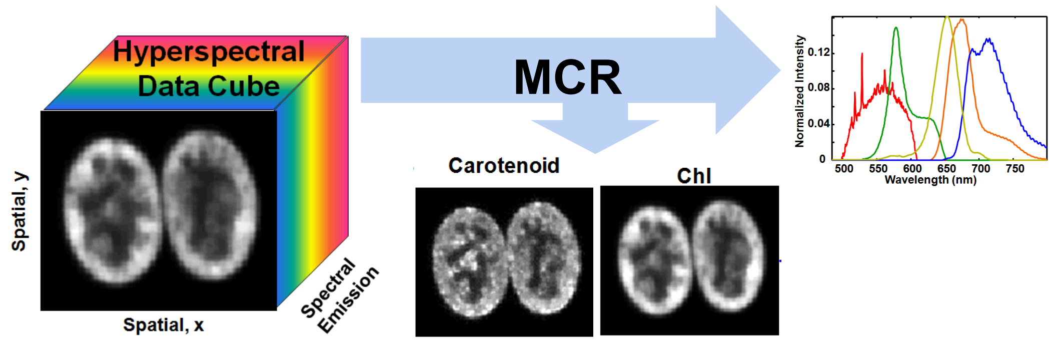
Current Projects

Building Hyperspectral STED



Adapted from Howard Vindin - Own work, CC BY-SA 4.0, https://commons.wikimedia.org/w/index.php?curid=40722030

Adding capabilities to Multivariate Curve Resolution (MCR), algorithm for extracting info from hyperspectral datasets.



Acknowledgements

Wavelet Detection @ UT Southwestern while in Ward-Ober Lab

Particle Tracking @ University of Illinois with Steve Granick & Kejia Chen

Hyperspectral STED @ Sandia National Labs with Jeri Timlin & Jesse Aaron

MCR @ Sandia National Labs building on work by Mark Van Benthem et al.

Sandia National Laboratories is a multi-program laboratory managed and operated by Sandia Corporation, a wholly owned subsidiary of Lockheed Martin Corporation, for the U.S. Department of Energy's National Nuclear Security Administration under contract DE-AC04-94AL85000. Support is acknowledged from Sandia National Laboratories' Laboratory Directed Research and Development project "Unmasking Hidden Compounds within Hyperspectral Images"