The Hanbury Brown and Twiss Experiment as a Tool for Emitter Localization

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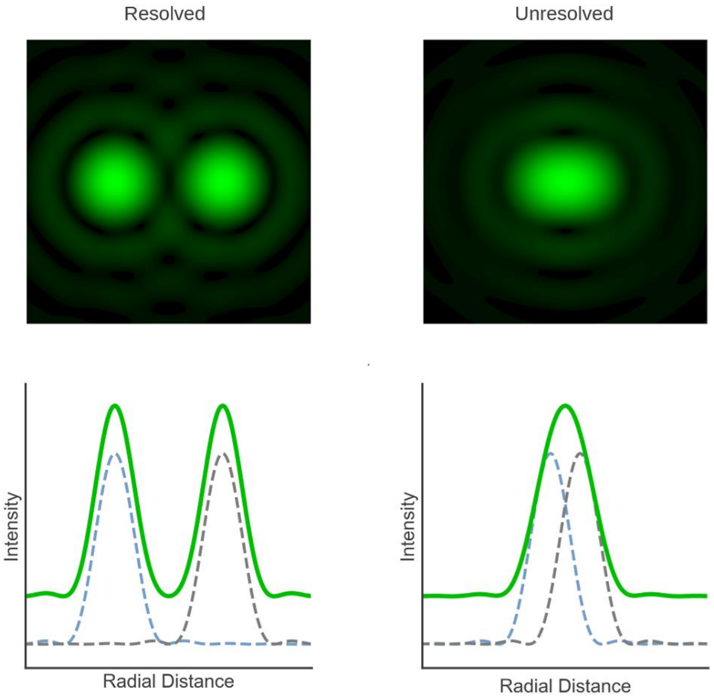
What's next…

Classical Diffraction Limit

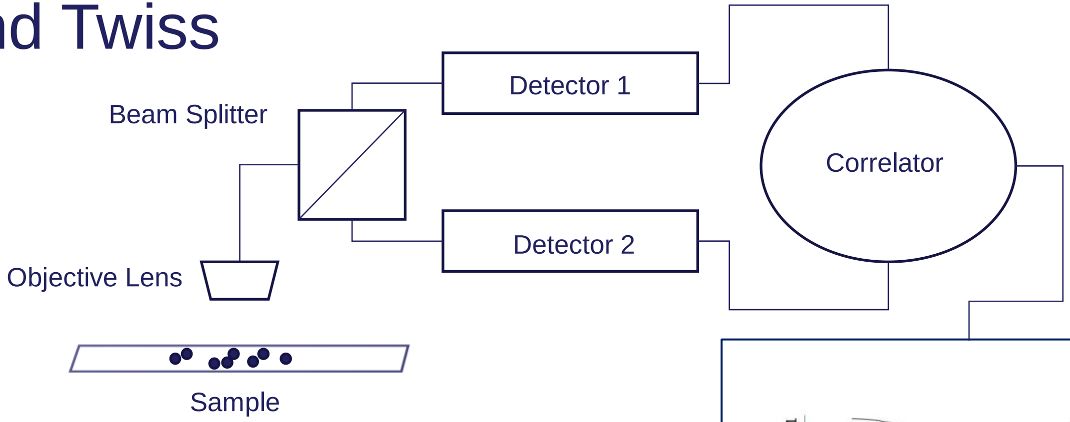
- Due to the wavelike nature of light, classical microscopy has a diffraction limit
- There are new, diffraction unlimited microscopy techniques (STED, STORM, etc.)
- High resolution techniques may damage samples due to amount of light needed

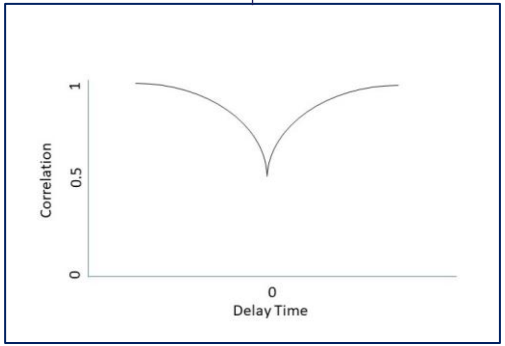


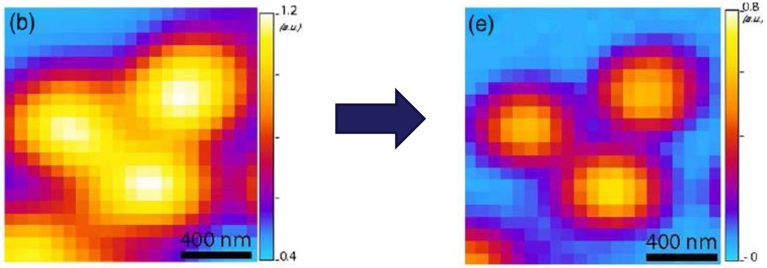
Edinburgh Instruments, *The Rayleigh Criterion for Microscope Resolution*, https://www.edinst.com/de/news/the-rayleigh-criterion-for-microscope-resolution/

Hanbury Brown and Twiss

- Quantum correlation microscopy can be used to increase resolution
- Hanbury Brown & Twiss measurement gives more information for less light







Monticone *et al*. (2014), Beating the Abbe Diffraction Limit in Confocal Microscopy via Nonclassical Photon Statistics, *Physical Review Letters* ***113***

HBT Second Order Correlation Function

- Can be done for N emitters
- P_i: our point spread function (represent the intensity from emitters)
- Can also consider background

$$g_N^{(2)} = \frac{2\sum_{i=1}^{N-1}\sum_{j=i+1}^{N} P_i P_j}{\sum_{i=1}^{N}\sum_{j=1}^{N} P_i P_j}$$

Worboys *et al.* (2020), Quantum multilateration: Subdiffraction emitter pair localization via three spatially separate Hanbury Brown and Twiss measurements, *Physical Review A* ***101***

We are interested in correlation where Delay time = 0:

$$g_N^{(2)}(0)$$

Expanded $g_N^{(2)}$ Functions (2 emitter version)

$$g^{(2)}_{2+bg}(0) = \frac{2(P_1P_2 + (P_1 + P_2)\mathcal{N}P_{bg} + \frac{(\mathcal{N}P_{bg})^2}{2})}{(P_1 + P_2)^2 + 2(P_1 + P_2)\mathcal{N}P_{bg} + (\mathcal{N}P_{bg})^2}.$$

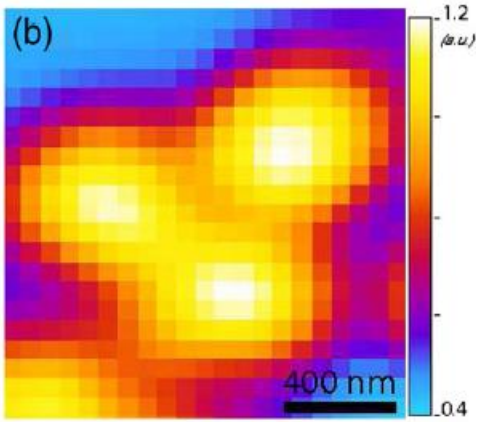
Background terms

$$g^{(2)}_{2+bg}(0) = \frac{2(c_{1,2} + (c_1 + c_2)\mathcal{N}c_{bg} + \frac{(\mathcal{N}c_{bg})^2}{2})}{(c_1 + c_2)^2 + 2(c_1 + c_2)\mathcal{N}c_{bg} + (\mathcal{N}c_{bg})^2}.$$

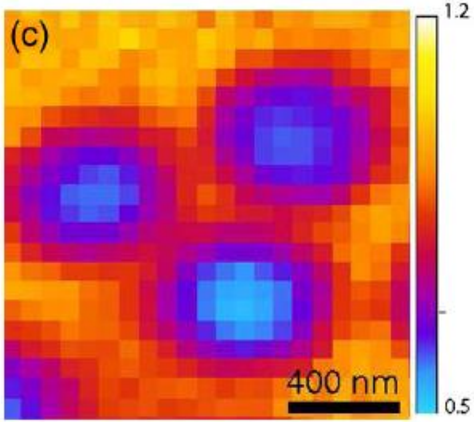
$$c_i = \mathrm{poissrnd}(P_i t)$$

Real measurement time dependant on brightness of emitters

Appearance of $g_N^{(2)}(0)$



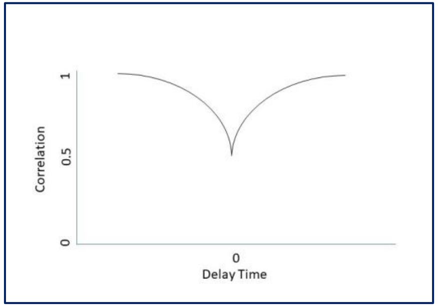
Intensity



$g_N^{(2)}(0)$

← $g_N^{(2)}(\infty) = 1$ (background)

← $g_3^{(2)}(0) = 0.67$

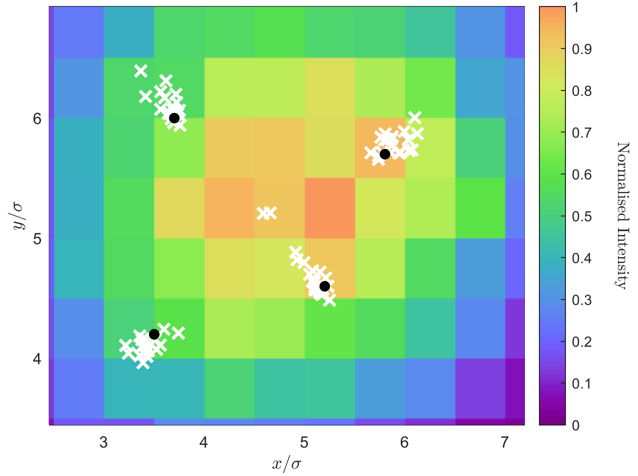


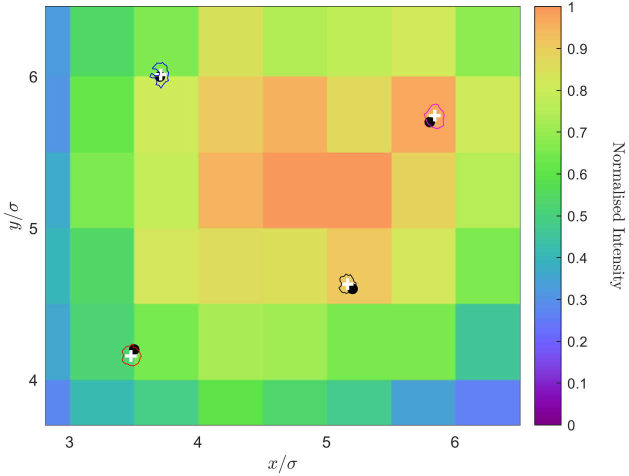
Monticone *et al*. (2014), Beating the Abbe Diffraction Limit in Confocal Microscopy via Nonclassical Photon Statistics, *Physical Review Letters* ***113***

Effective Point Spread Function: ω_{eff}

- We collect the results that are closest within an area up to the 39.5th result (i.e. standard deviation)

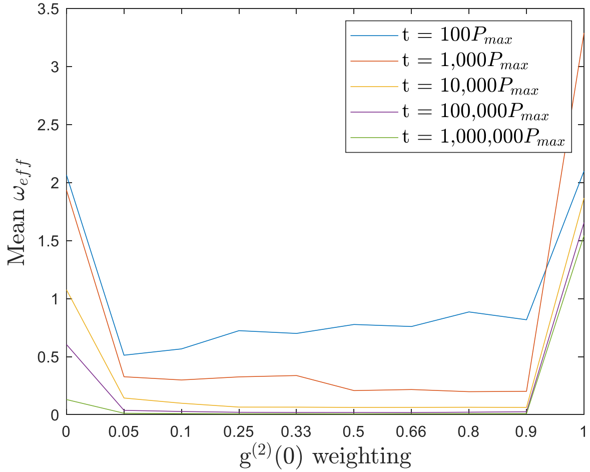
- We construct a polygon connecting those results

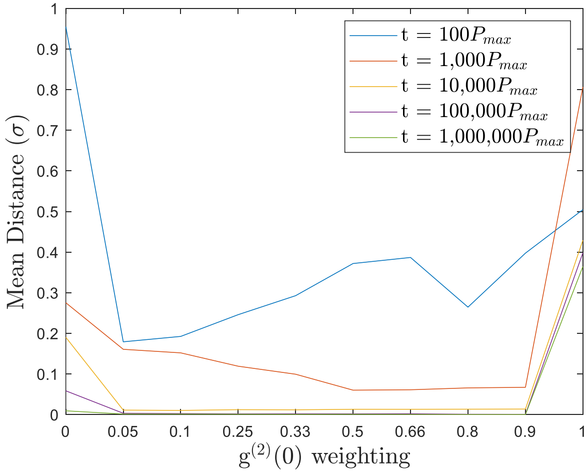




Residual Sum of Squares and Weighting

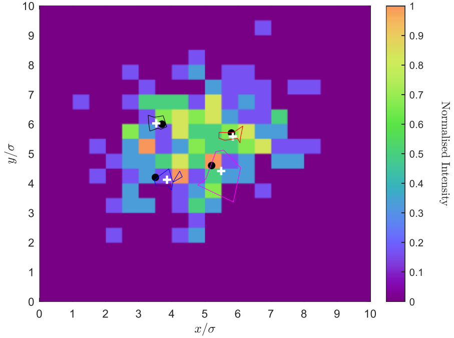
$$RSS = \alpha RSS_{Intensity} + \beta RSS_{Correlation}$$





Effects of Increasing Measurement Time

t = 10 $P_{i,0}$



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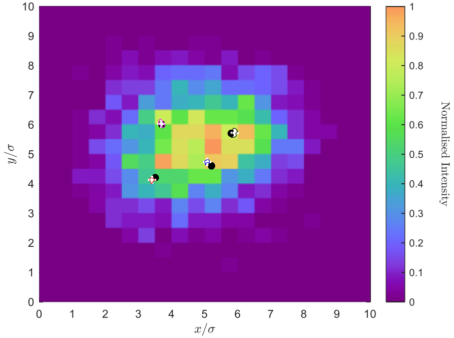

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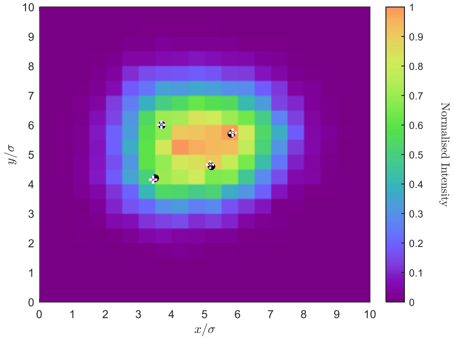
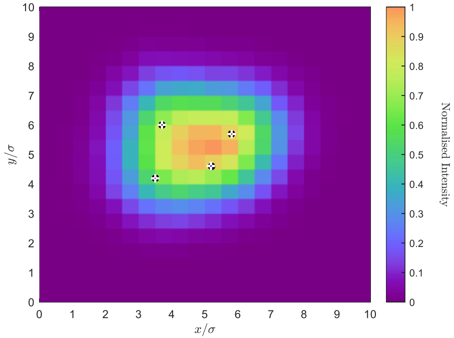
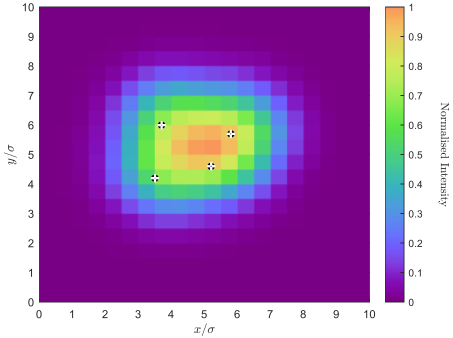


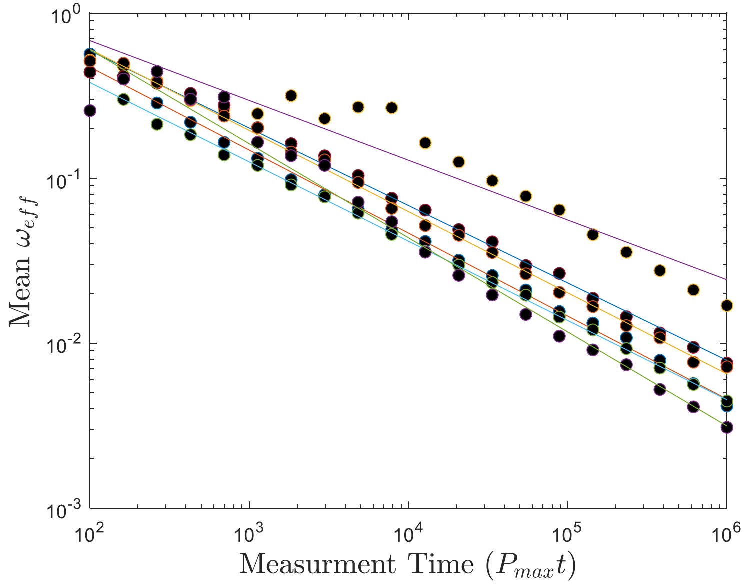
t = 10000 $P_{i,0}$



t = 100000 $P_{i,0}$



Time Scaling Laws



Slopes for configurations are approximately -0.5 as expected ($1/\sqrt{t}$).

$$y = x^{slope} exp^{intercept}$$

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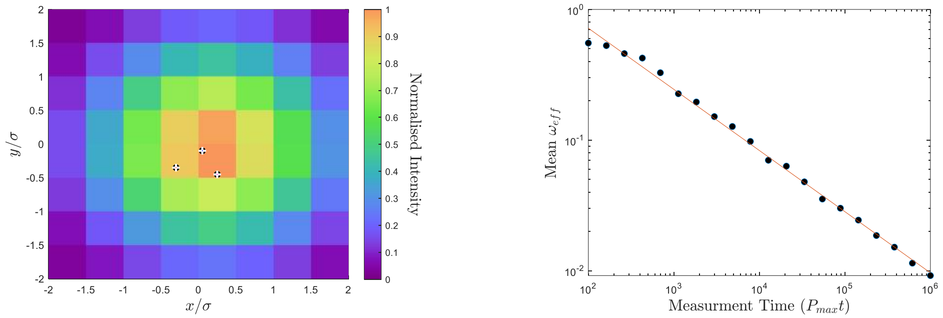
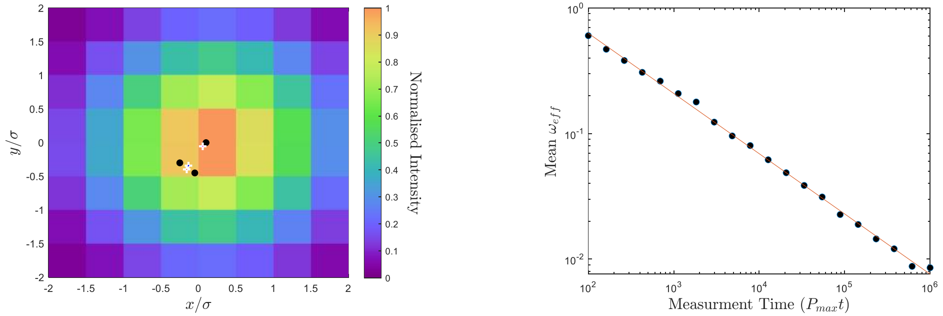
Time Scaling With Unequal Brightness and Background

- We can still expect $1/\sqrt{t}$ scaling



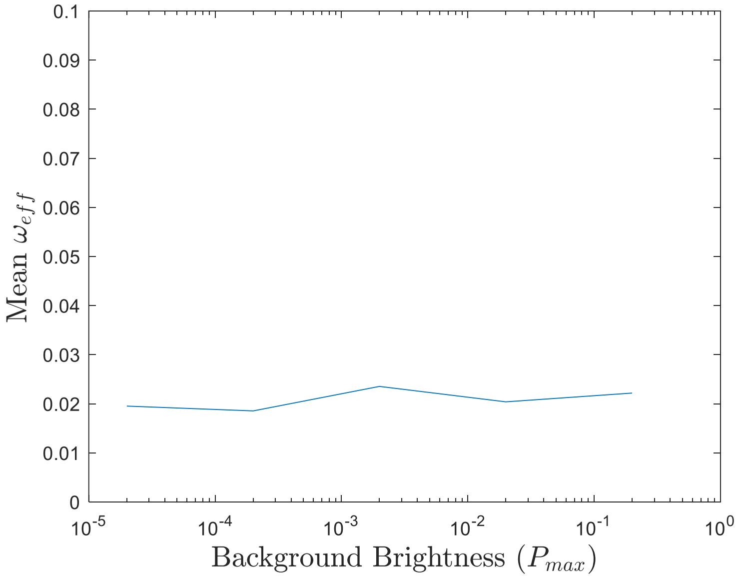
Slope:
-0.4681

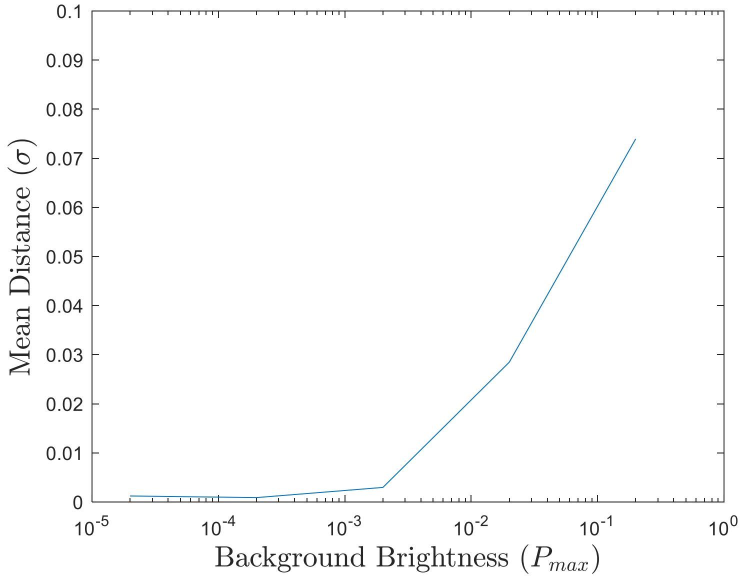


Slope:
-0.4797

BG = 20%

Effects of Increasing Background Brightness





Akaike Information Criteria

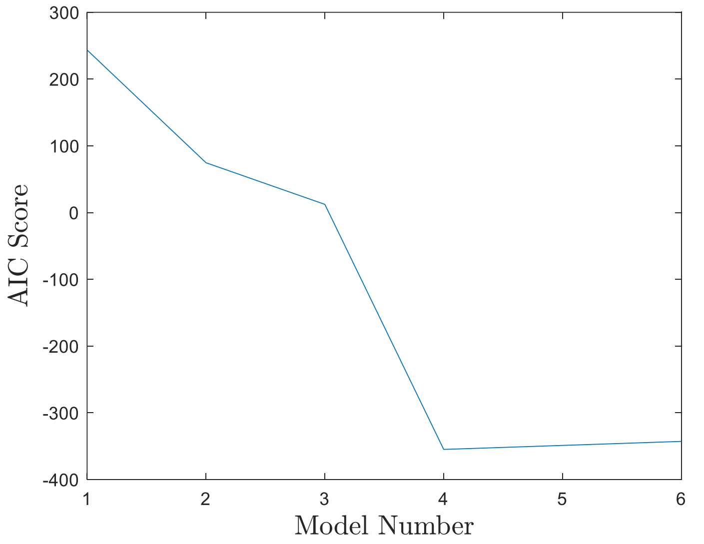
$$AIC = \underbrace{2k}_{\text{}} - \underbrace{2ln(\hat{L})}_{\text{}}$$

Penalty term

Likelihood function

Modified to use RSS:

$$AIC = 2k + nln(RSS)$$



AIC scoring of configuration with 4 emitters. Model Number corresponds to number of emitters being used to fit data. Lower score corresponds to better model.

Akaike, H (1992), Information Theory and an Extension of the Maximum Likelihood Principle, *Breakthroughs in Statistics: Foundations and Basic Theory. Pages 610-624*

Burnham K., Anderson D., (2004), Multimodal Interference: Understanding AIC and BIC in Model Collection, *Sociological Methods & Research 2004 Vol. 33 Issue 2 Pages 261-304*

Akaike Information Criteria – Part 2

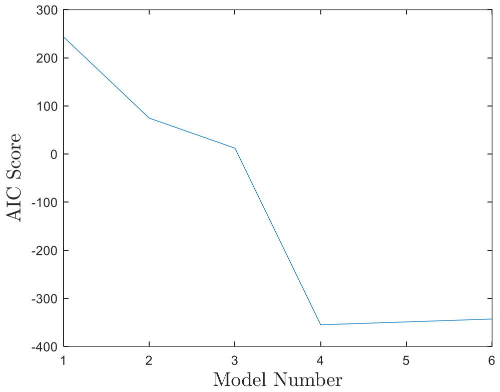
Likelihood of minimizing information loss:

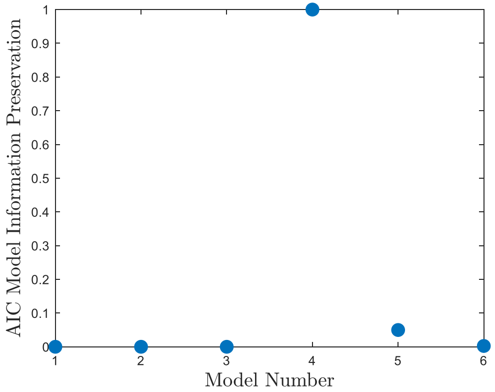
$$\exp\left(\frac{AIC_{min} - AIC_i}{2}\right)$$

A small difference between AIC scores may seem trivial (e.g. -360 vs -350), but it is this small difference that is interpretable since AIC has large scaling constants.

(AIC 4: 1.00)

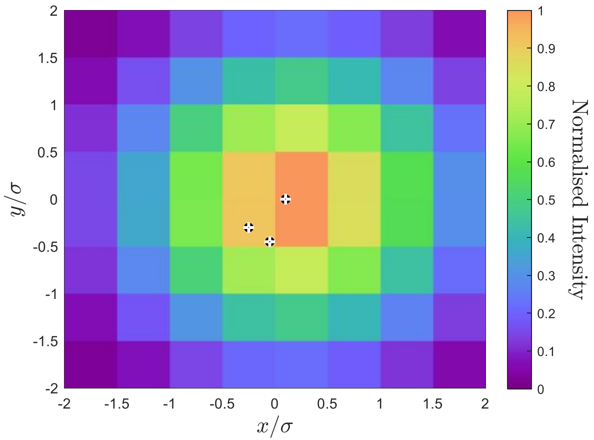
AIC 4 vs AIC 5: 0.0351
AIC 4 vs AIC 6: 0.0014

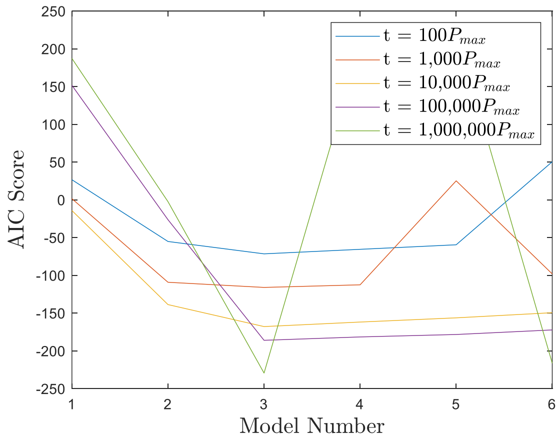


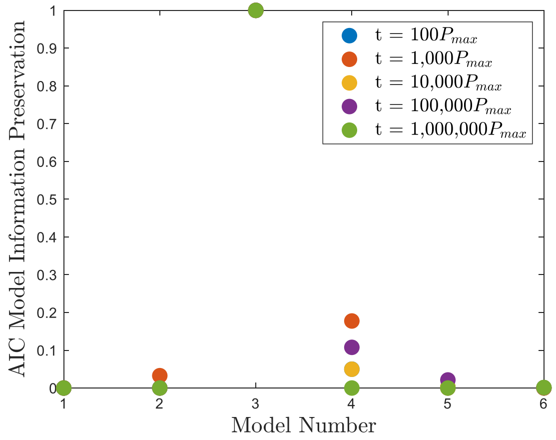


AIC for Predicting Emitter Amounts

- Could be used to help determine the number of emitters located in an ambiguous region







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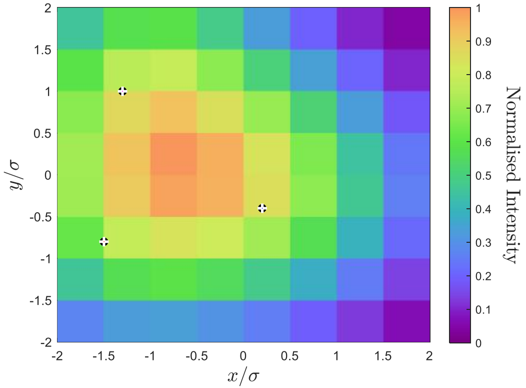
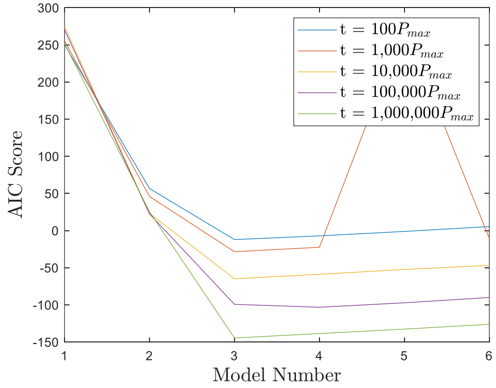
AIC with Ambiguous Emitter Amounts

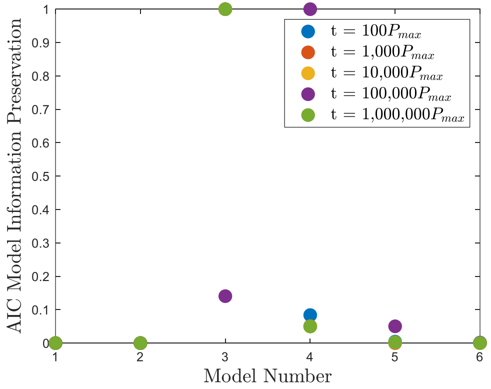
- Ambiguous cases can still occur. May not be viable to use AIC as the only tool for emitter number estimation

- Can be caused by close emitters, far emitters and high backgrounds

Here, for some time steps, models with the incorrect number of emitters are predicted







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