Multiscale Scanning in Inverse Problems: Applications to super-resolution microscopy

Frank Werner

joint with

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and

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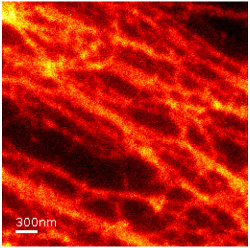
University of Göttingen

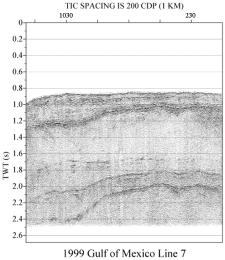
Localization in imaging modalities

In many imaging modalities one observes a **noisy** and **blurred** version of the underlying truth!

Astrophysics



Fluorescence microscopy



Reflection seismology

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Statistical model

Observations

$$Y_{\mathbf{j}} = (f * k)(s_{\mathbf{j}}) + \xi_{\mathbf{j}}, \quad \mathbf{j} \in \{1, \ldots, n\}^d.$$

with

- the underlying truth $f \geq 0$ (stars / galaxies, fluorescent dyes, seismic sources),
- the kernel k (**blur**, **psf**, ...),
- the convolution $(f * k)(s) = \int k(s - y) f(y) \, \mathrm{d}y$,
- independent and centered rvs $\xi_{\mathbf{j}}$, $\mathbf{j} \in \{1, \ldots, n\}^d$ (**noise**),
- and sampling points $s_{\mathbf{j}} \in \mathbb{R}^d$, $\mathbf{j} \in \{1, \ldots, n\}^d$.

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We will regard this as the multiple testing problem

$$H_B : \quad f_{|_B} \equiv 0 \qquad \text{vs.} \qquad K_B : \quad f_{|_B} \not\equiv 0$$

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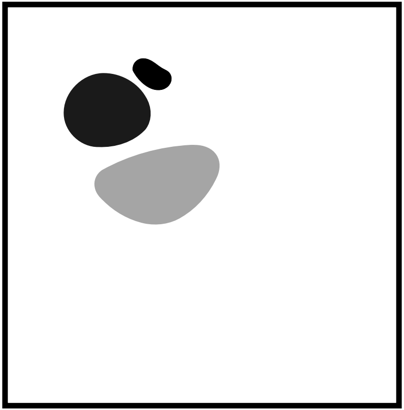
Detection will be done at controlled **family-wise error rate** (FWER):

$$\sup_{B \in \mathcal{B}} \mathbb{P}_{H_B} \left[H_B \text{ is rejected} \right] \leq \alpha + o(1) \qquad \text{as} \qquad n \to \infty.$$

Statistical scanning



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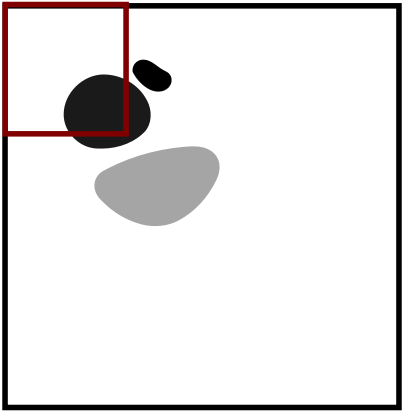

- Detection of **weak signal** requires **large boxes**

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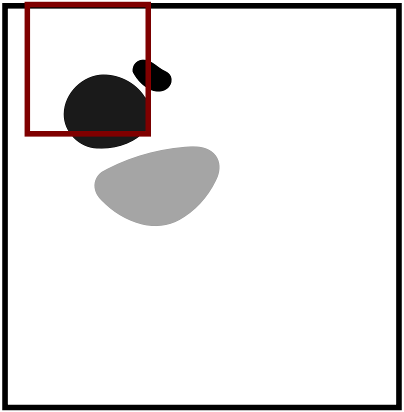

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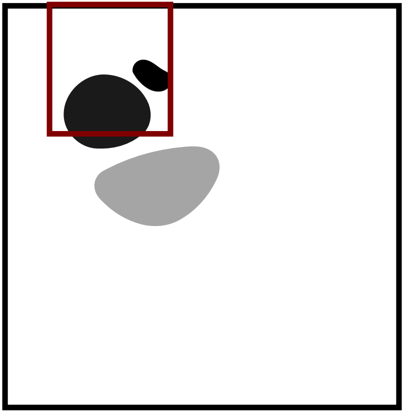

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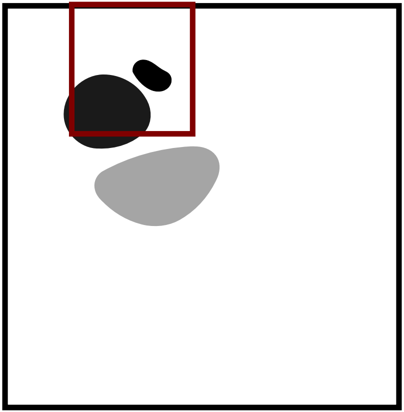

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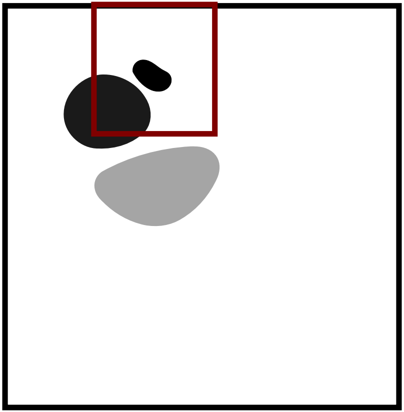

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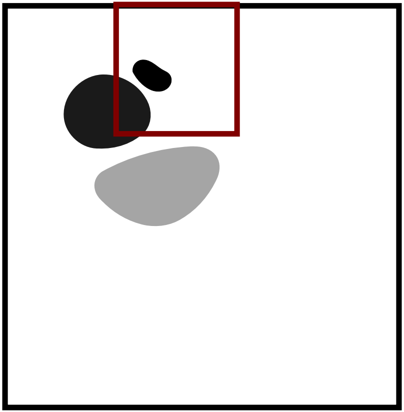

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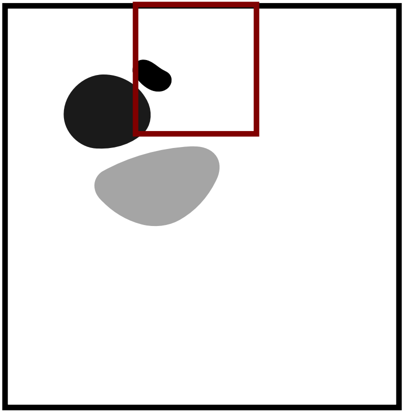

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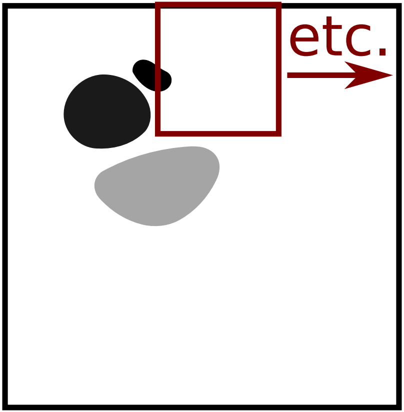

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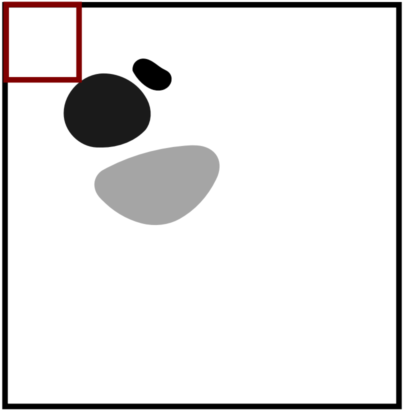

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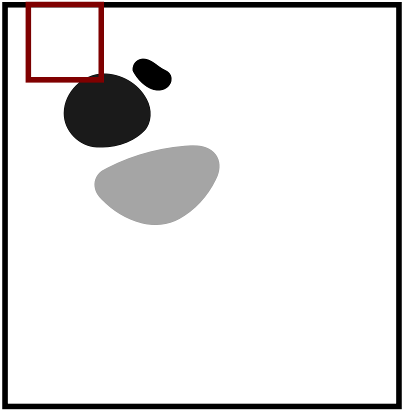

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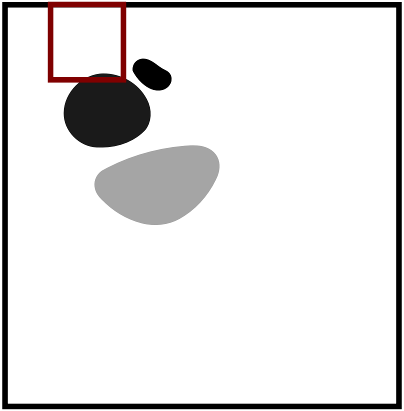

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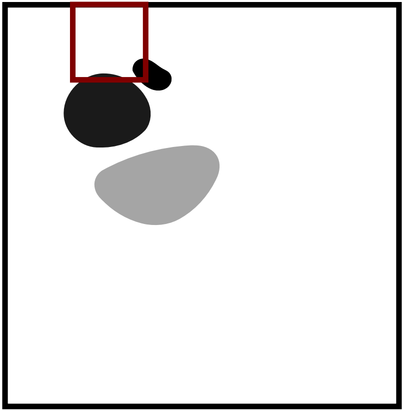

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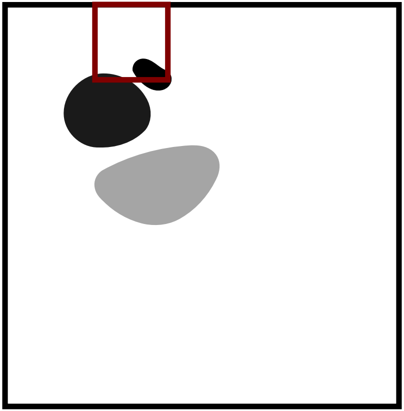

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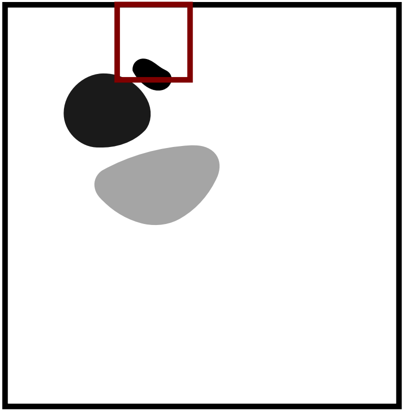

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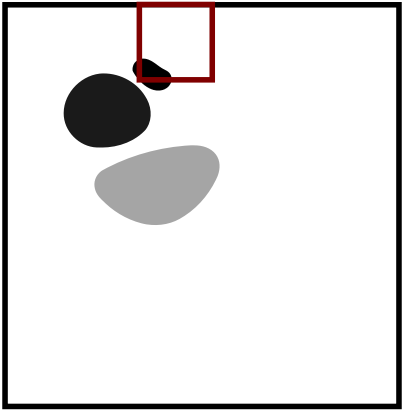

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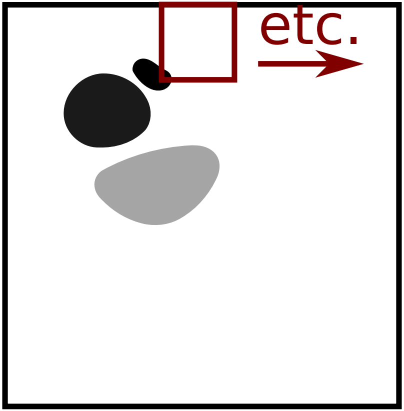

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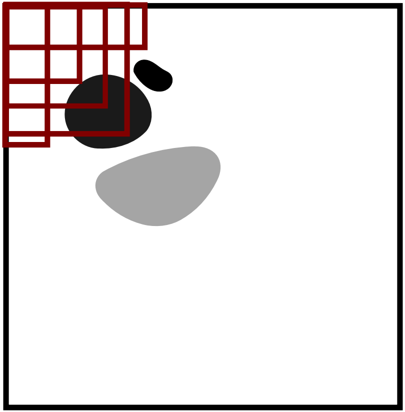
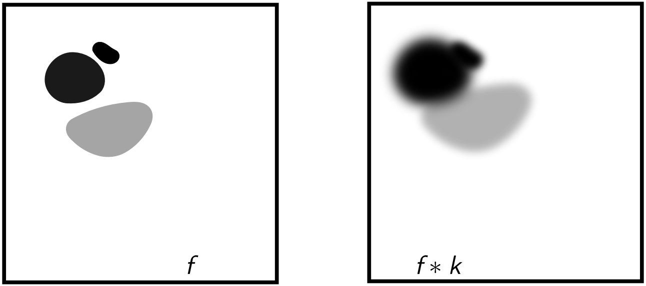


- As signal strength **varies locally**, we use **many different sizes of boxes**

But: convolution introduces problems ...



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- small structures are smeared out

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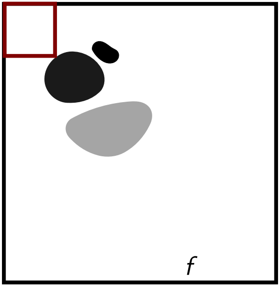

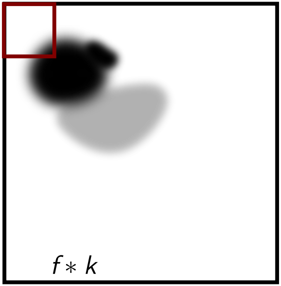

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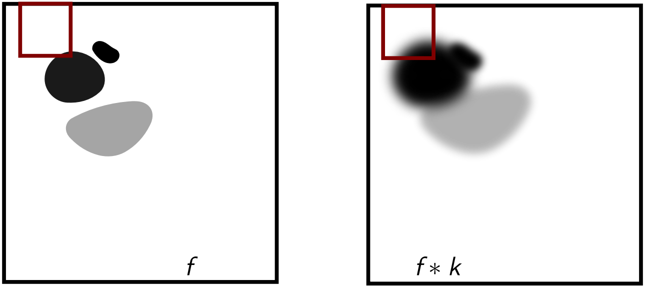

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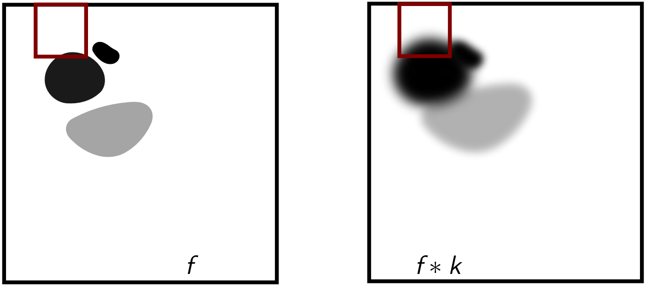

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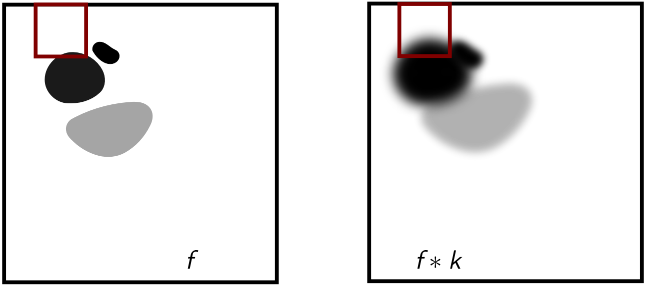

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⇝ loss of information!

How to 'scan' in deconvolution problems?

Statistical scanning in deconvolution problems

- For each box $B \in \mathcal{B}$, choose a suitable function φ_B with $\text{supp}(\varphi_B) = B$, $\varphi_B \geq 0$. Then

$$\langle \varphi_B, f \rangle > 0 \qquad \Leftrightarrow \qquad f_{|_B} \not\equiv 0$$

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- Consequently, we **scan over** f by means of $\{\varphi_B\}_{B \in \mathcal{B}}$ **by scanning over** $f * k$ by means of $\{\Phi_B\}_{B \in \mathcal{B}}$
- The local test statistics are combined to the global scan statistic

$$T_n(Y) = \max_{B \in \mathcal{B}} \left[w_B \left(\frac{\langle \Phi_B, Y \rangle}{\sqrt{\mathbf{Var}\left[\langle \Phi_B, Y \rangle\right]}} - w_B \right) \right].$$

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Is $T_B(Y) > \left(\frac{q_{1-\alpha}}{w_B} + w_B \right) \sqrt{\mathbf{Var}\left[T_B(Y)\right]}$?

Yes → **Mark B as active**

No → Do not mark B as active

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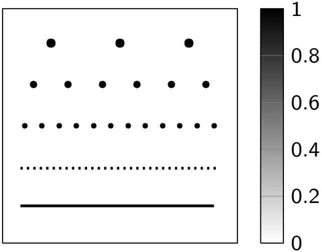
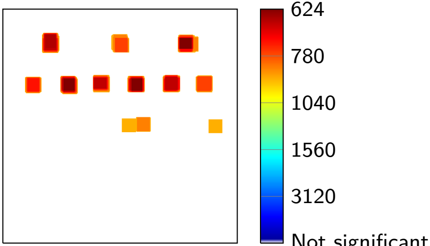
⇝ max ensures FWER $\leq \alpha$, this is

all active B are 'correct' with probability $\geq 1 - \alpha$

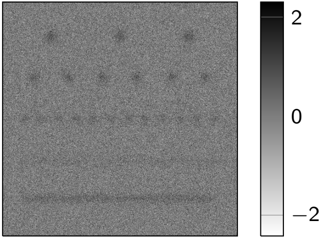
Performance in simulations



testfunction



resulting significance map (90% confidence)



simulated data, $\sigma = 0.5$

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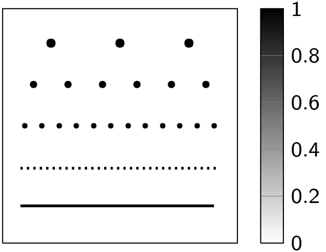

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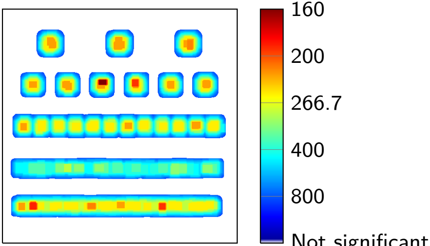

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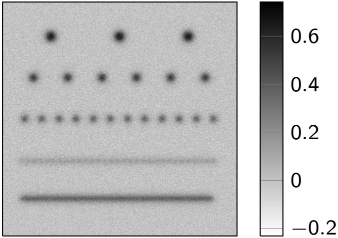

simulated data, $\sigma = 0.05$

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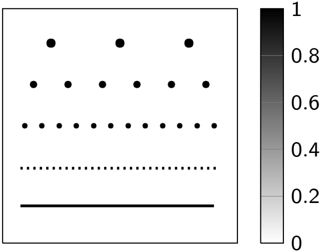

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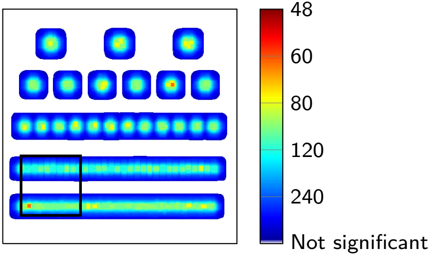

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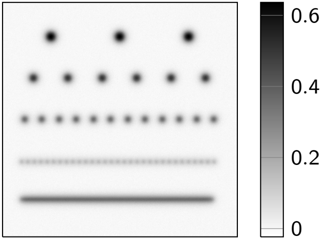
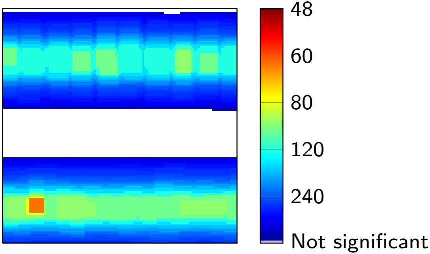


simulated data, $\sigma = 0.005$



zoom

Application to super-resolution microscopy

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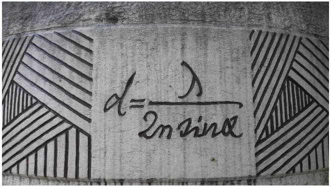
Abbe's diffraction limit: **light cannot be focused to a point**!



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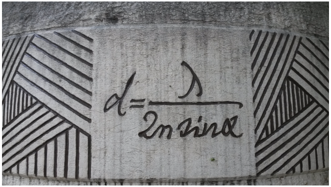

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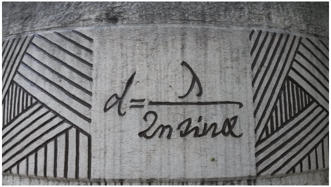

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However, **super-resolution is possible**!

Application to super-resolution microscopy

The Nobel Prize in Chemistry 2014

Photo: Matt Staley/HHMI

Eric Betzig

Prize share: 1/3

Photo: Wikimedia Commons, CC-BY-SA-3.0

Stefan W. Hell

Prize share: 1/3

Photo: K. Lowder via Wikimedia Commons, CC-BY-SA-3.0

William E. Moerner

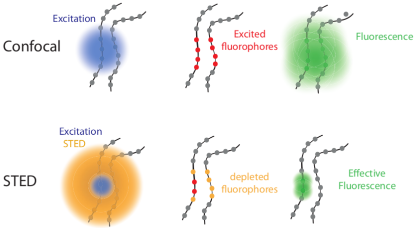
Prize share: 1/3

”for the development of super-resolved fluorescence microscopy”

Application to super-resolution microscopy

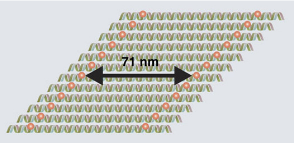
"for the development of super-resolved fluorescence microscopy"

Here we rely on **STimulated Emission Depletion (STED)**, developed by Hell & Wichmann '94

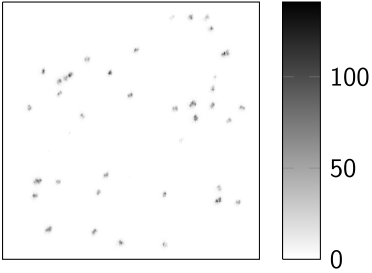


Application to super-resolution microscopy

- we analyze fluorescent dyes on single DNA Origami
- each of the two strands can at most hold 12 markers



Photon counts by STED:



Data kindly provided by Haisen Ta, Hell Lab

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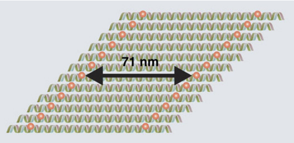
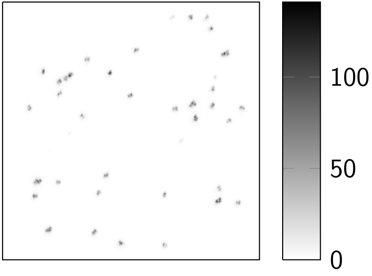
- we analyze fluorescent dyes on single DNA Origami
- each of the two strands can at most hold 12 markers



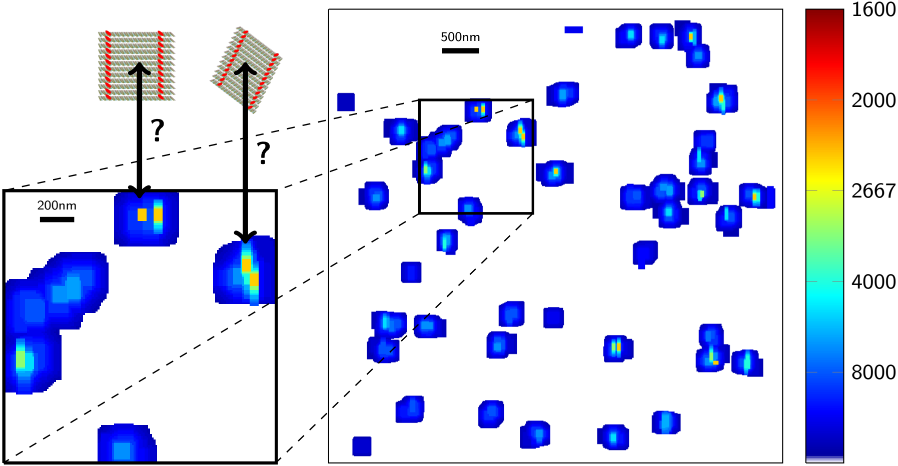
Photon counts by STED:



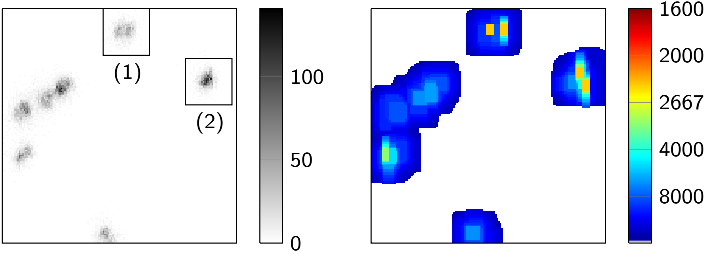
Data kindly provided by Haisen Ta, Hell Lab

Model $Y_j \sim \textbf{Bin}\left(t, (f * k)(s_j)\right)$ with $f \hat{=}$ density of fluorescent dyes, $k \hat{=}$ point spread function, $t \hat{=}$ number of illumination pulses

Resulting significance map (90% confidence)

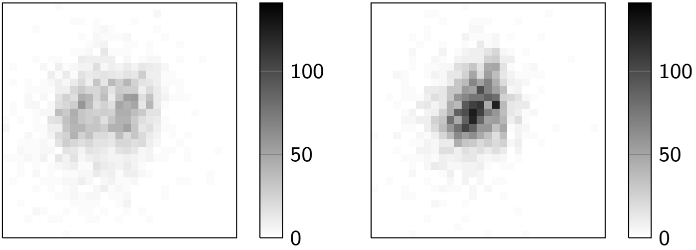


Comparison of the result with the data



data excerpt

result excerpt



zoomed data (1)

zoomed data (2)

Conclusion and outlook

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K. Proksch, F. Werner and A. Munk: Multiscale Scanning in Inverse Problems. To appear in *Ann. Stat.*, arXiv:1611.04537.

Thank you for your attention!