Blind deconvolution of 3D data in wide field fluorescence microscopy

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ISBI 2012

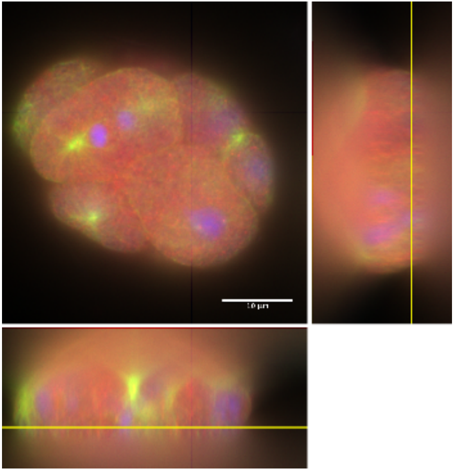
Wide Field Fluorescence Microscopy

- Uniform illumination of the whole specimen,
- Imaging at the emission wavelenght,
- Moving the focal plane produces a 3D representation of the specimen.

Coarse depth resolution

Improving resolution

- Improving PSF (confocal, multiphoton. . .),
- single molecule microscopy,
- Deconvolution.



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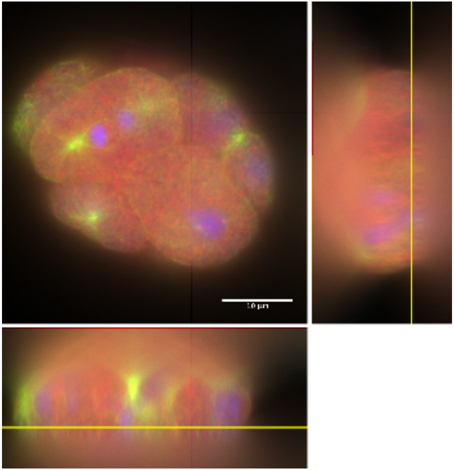

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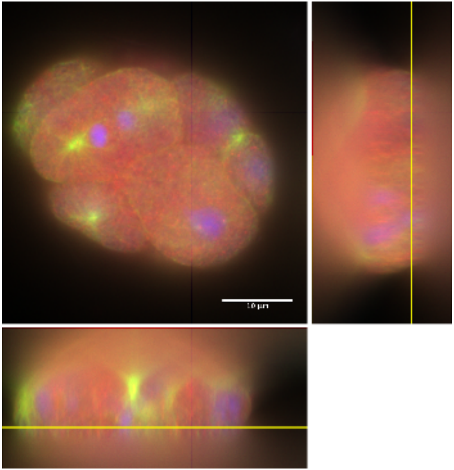

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Blind deconvolution

Blur modeled by a convolution : $\boldsymbol{y} = \boldsymbol{h} * \boldsymbol{x} + \boldsymbol{n}$

Deconvolution :
Estimating the *crisp image* $\boldsymbol{x}$ of the specimen given the *data* $\boldsymbol{y}$, the *PSF* $\boldsymbol{h}$ and the *noise* $\boldsymbol{n}$ statistics.
See [Agard & Sedat, 1983], [Sibarita, 2005] and [Sarder, 2005].

But : The PSF is not known

- theoretical diffraction-limited PSF — no flexibility
- measured PSF with calibration beads — complex, noisy
- estimated directly from the blurred images — **Blind deconvolution**

Previous works by [Markam et al. 1999], [Hom et al. 2007] and [Kenig et al. 2010].

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Maximum a posteriori blind deconvolution

- Estimating the most probable couple *Object/PSF* $\{\boldsymbol{x}^+, \boldsymbol{h}^+\}$ according to the data and some *a priori* knowledge.
- Done by the minimisation of a cost function $\mathcal{J}(\boldsymbol{x}, \boldsymbol{h})$:

$$\mathcal{J}(\boldsymbol{x}, \boldsymbol{h}) = \underbrace{\mathcal{J}_{\text{data}}(\boldsymbol{x}, \boldsymbol{h})}_{\text{likelihood}} + \mu \underbrace{\mathcal{J}_{\text{prior}}(\boldsymbol{x})}_{\text{object priors}},$$

PSF priors enforced by its parametrization.

Object a priori globally smooth with few sharp edges :
Hyperbolic approximation of 3D total variation :

$$\mathcal{J}_{\text{prior}}(\boldsymbol{x}) = \sum_k \sqrt{\|\nabla x_k\|_2^2 + \epsilon^2}\,.$$

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Likelihood

- Gaussian noise :

$$\mathcal{J}_{\text{data}}(\boldsymbol{x}) = \frac{1}{2}(\boldsymbol{y} - \mathbf{H}\cdot\boldsymbol{x})^{\mathrm{T}} \cdot \mathbf{C}_{\text{noise}}^{-1} \cdot (\boldsymbol{y} - \mathbf{H}\cdot\boldsymbol{x})$$

- Uncorrelated non-stationnary Gaussian noise :

$$\mathcal{J}_{\text{data}}(\boldsymbol{x}) = \sum_{k=Pixels} \sum_{\lambda} \frac{1}{\sigma_{k,\lambda}} \left[(\mathbf{H}\cdot\boldsymbol{x})_k - y_{k,\lambda}\right]^2$$

  Missing pixels k $\longrightarrow \sigma_{k,\lambda} = \infty$.

- Poisson Noise $\approx$ non-stationnary Gaussian noise

$$\sigma_{k,\lambda} = \gamma(\mathbf{H}\cdot\boldsymbol{x})_{k,\lambda} + \sigma^2_{\mathrm{CCD}} \approx \gamma \max(y_{k,\lambda}, 0) + \sigma^2_{\mathrm{CCD}}$$

  where γ is a quantization factor and σ^2_{CCD} account for Gaussian additive noise (*e.g.* readout noise).

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PSF parametrization

PSF $\boldsymbol{h}$ defined as a function of the pupil function as *Markham (1999)*

$$h(\boldsymbol{r}_j, z) = \left|\sum\nolimits_k F_{j,k}\, a_k(z)\right|^2 ,$$

with $\boldsymbol{r}_j$ lateral position of pixel j, $\mathbf{F}$ discrete Fourier transform and $a_k(z)$ pupil function at frequel k and depth z.

$$a_k(z) = \rho_k \, \exp(\mathrm{i}\, 2\,\pi\,(\phi_k + z\,\psi_k)) ,$$

$$\rho_k = \sum\nolimits_n \beta_n Z_k^n ,$$

$$\phi_k = \sum\nolimits_n \alpha_n Z_k^n ,$$

$$\psi_k = \sqrt{(n_\mathrm{i}/\lambda)^2 - \|\kappa_k\|^2}$$

where Z_k^n the n-th Zernike polynomial [Hanser 2004] and n_i the refractive index of immersion medium.

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PSF parametrization

Preventing some degeneracies :

- Centering PSF : removing phase tip-tilt $\alpha_1 = \alpha_2 = 0$.
- normalizing PSF $\int h(k) \mathrm{d}k = 1$: constraining $\sum_n \beta_n^2 = 1$.

Benefits of such parametrization :

- optically derived model,
- require only the knowledge of the wavelength λ, the numerical aperture NA,
- few parameters (several tenth),
- no additional priors (regularization),
- ensure PSF positivity,
- taking only radial Zernike polynomials ensure axially symmetric PSF.

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Algorithm summary

Solution given by :

$$\{\boldsymbol{x}^+, n_i^+, \boldsymbol{\alpha}^+, \boldsymbol{\beta}^+\} = \arg\min_{\boldsymbol{x}, n_i, \boldsymbol{\alpha}, \boldsymbol{\beta}} \left\{ \mathcal{J}_{\text{data}}(\boldsymbol{x}, \boldsymbol{h}(n_i, \boldsymbol{\alpha}, \boldsymbol{\beta}; \boldsymbol{y})) + \mu\, \mathcal{J}_{\text{prior}}(\boldsymbol{x}) \right\}$$

Non-convex and badly conditioned problem.

Alternating minimization :

- Begin with aberrations free PSF $h^{(0)}$ ($\alpha = \beta = 0$), set $n = 1$:
  1. $\boldsymbol{x}^{(n)} = \arg\min_{\boldsymbol{x}} \left\{ \mathcal{J}_{\text{data}}(\boldsymbol{x}, \boldsymbol{h}^{(n-1)}; \boldsymbol{y}) + \mu\, \mathcal{J}_{\text{prior}}(\boldsymbol{x}) \right\}$
  2. $n_i^{(n)} = \arg\min_{n_i} \mathcal{J}_{\text{data}}(\boldsymbol{x}^{(n)}, \boldsymbol{h}(n_i, \boldsymbol{\alpha}^{(n-1)}, \boldsymbol{\beta}^{(n-1)}); \boldsymbol{y})$
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  5. $n = n + 1$, go to step 1
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  3. $\boldsymbol{\alpha}^{(n)} = \underset{\boldsymbol{\alpha}}{\arg\min} \mathcal{J}_{\text{data}}(\boldsymbol{x}^{(n)}, \boldsymbol{h}(n_i^{(n)}, \boldsymbol{\alpha}, \boldsymbol{\beta}^{(n-1)}); \boldsymbol{y})$
  4. $\boldsymbol{\beta}^{(n)} = \underset{\boldsymbol{\beta}}{\arg\min} \mathcal{J}_{\text{data}}(\boldsymbol{x}^{(n)}, \boldsymbol{h}(n_i^{(n)}, \boldsymbol{\alpha}^{(n)}, \boldsymbol{\beta}; \boldsymbol{y})$ under constraint $\sum_k \beta_k^2 = 1$.
  5. $n = n + 1$, go to step 1
- until a certain convergence.

Algorithm summary

Solution given by :

$$\{\boldsymbol{x}^+, n_i^+, \boldsymbol{\alpha}^+, \boldsymbol{\beta}^+\} = \arg\min_{\boldsymbol{x}, n_i, \boldsymbol{\alpha}, \boldsymbol{\beta}} \left\{ \mathcal{J}_{\text{data}}(\boldsymbol{x}, \boldsymbol{h}(n_i, \boldsymbol{\alpha}, \boldsymbol{\beta}; \boldsymbol{y})) + \mu \mathcal{J}_{\text{prior}}(\boldsymbol{x}) \right\}$$

Non-convex and badly conditioned problem.
Alternating minimization :

- Begin with aberrations free PSF $h^{(0)}$ ($\boldsymbol{\alpha} = \boldsymbol{\beta} = 0$), set $n = 1$:
  1. $\boldsymbol{x}^{(n)} = \arg\min_{\boldsymbol{x}} \left\{ \mathcal{J}_{\text{data}}(\boldsymbol{x}, \boldsymbol{h}^{(n-1)}; \boldsymbol{y}) + \mu \mathcal{J}_{\text{prior}}(\boldsymbol{x}) \right\}$
  2. $n_i^{(n)} = \arg\min_{n_i} \mathcal{J}_{\text{data}}(\boldsymbol{x}^{(n)}, \boldsymbol{h}(n_i, \boldsymbol{\alpha}^{(n-1)}, \boldsymbol{\beta}^{(n-1)}); \boldsymbol{y})$
  3. $\boldsymbol{\alpha}^{(n)} = \arg\min_{\boldsymbol{\alpha}} \mathcal{J}_{\text{data}}(\boldsymbol{x}^{(n)}, \boldsymbol{h}(n_i^{(n)}, \boldsymbol{\alpha}, \boldsymbol{\beta}^{(n-1)}); \boldsymbol{y})$
  4. $\boldsymbol{\beta}^{(n)} = \arg\min_{\boldsymbol{\beta}} \mathcal{J}_{\text{data}}(\boldsymbol{x}^{(n)}, \boldsymbol{h}(n_i^{(n)}, \boldsymbol{\alpha}^{(n)}, \boldsymbol{\beta}; \boldsymbol{y})$ under constraint $\sum_k \beta_k^2 = 1$.
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- until a certain convergence.

Algorithm summary

Solution given by :

$$\{\boldsymbol{x}^+, n_i^+, \boldsymbol{\alpha}^+, \boldsymbol{\beta}^+\} = \underset{\boldsymbol{x}, n_i, \boldsymbol{\alpha}, \boldsymbol{\beta}}{\arg\min} \left\{ \mathcal{J}_{\text{data}}(\boldsymbol{x}, \boldsymbol{h}(n_i, \boldsymbol{\alpha}, \boldsymbol{\beta}; \boldsymbol{y})) + \mu \, \mathcal{J}_{\text{prior}}(\boldsymbol{x}) \right\}$$

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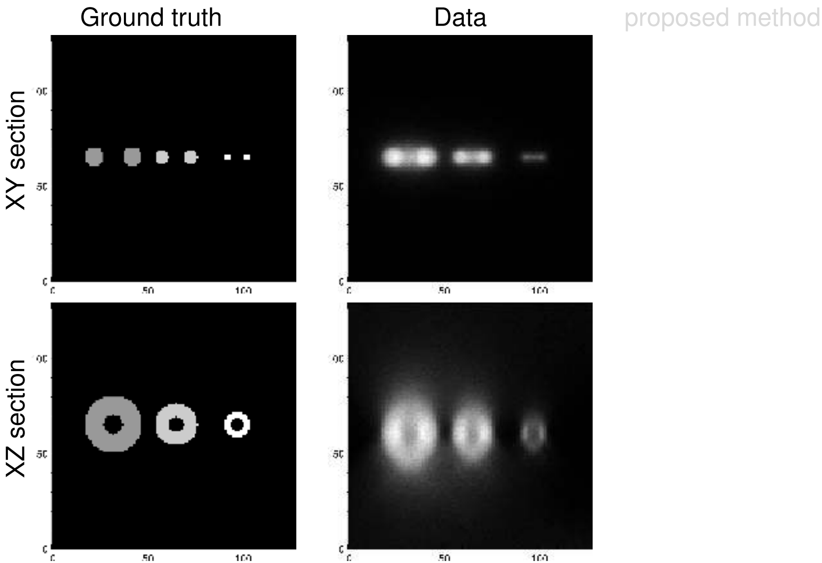
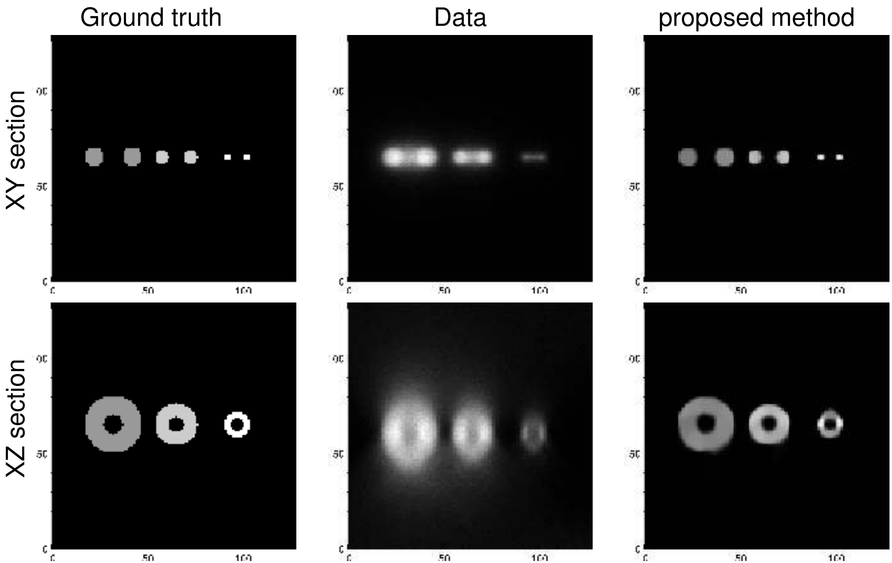
Blind deconvolution on simulations



Simulation with depth aberrations from *Kenig, Kam & Feuer, TPAMI, (2010)*

Blind deconvolution on simulations



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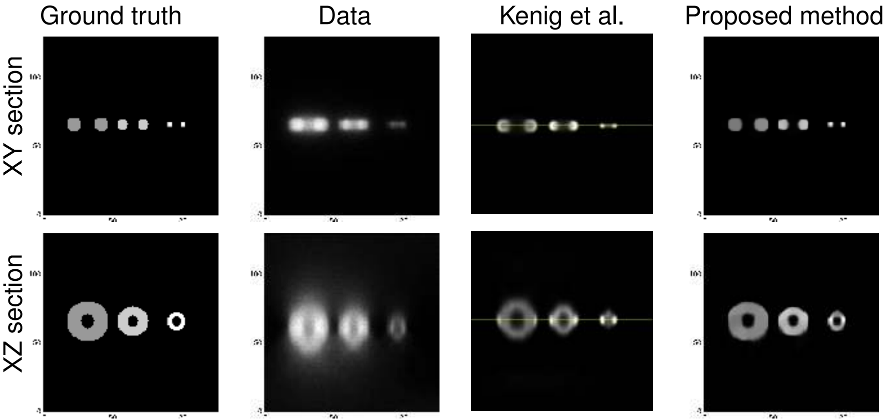
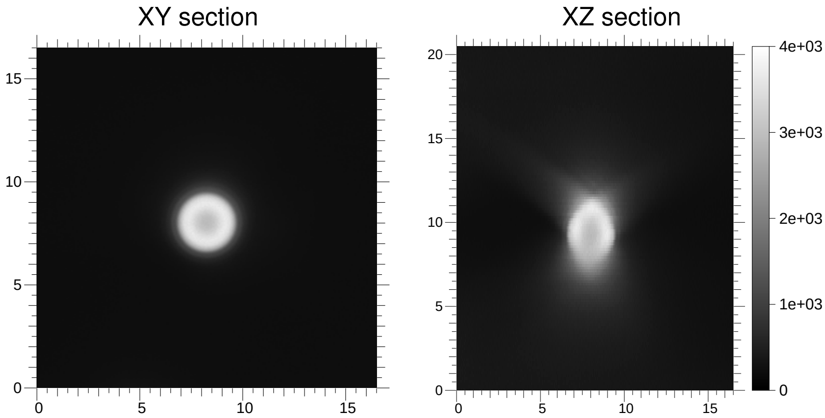
Blind deconvolution on simulations



RMSE	36.16	24.88	11.27

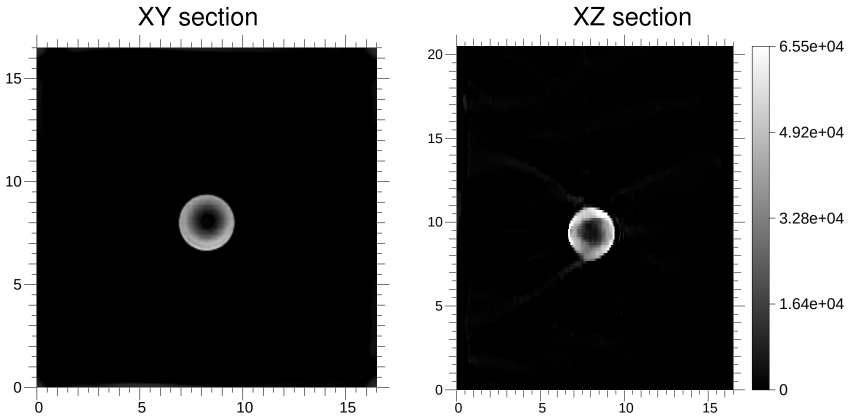
Simulation with depth aberrations from *Kenig, Kam & Feuer, TPAMI, (2010)*

Experimental results: Calibration bead



— Bead diameter: $2.5\mu m$, $NA = 1.4$
— 256^3 pixels $64.5 \times 64.5 \times 160nm^3$
from *A. Griffa, N. Garin & D. Sage, G.I.T. Imaging & Microscopy, 2010.*

Non blind deconvolution with theoretical PSF

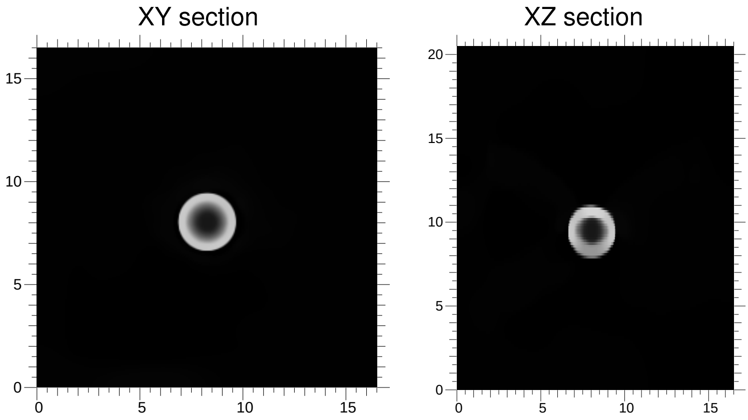


— Bead diameter: $2.5\mu m$, $NA = 1.4$, $\lambda = 512nm$

— 256^3 pixels $64.5 \times 64.5 \times 160nm^3$

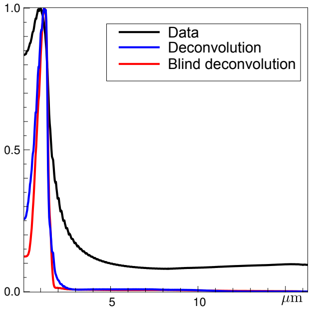
from *A. Griffa, N. Garin & D. Sage, G.I.T. Imaging & Microscopy, 2010.*

Calibration bead : blind deconvolution



— Bead diameter: $2.5\mu\text{m}$, $\text{NA} = 1.4$, $\lambda = 512\text{nm}$
— 256^3 voxels $64.5 \times 64.5 \times 160\text{nm}^3$
from *A. Griffa, N. Garin & D. Sage, G.I.T. Imaging & Microscopy, 2010.*

Calibration bead

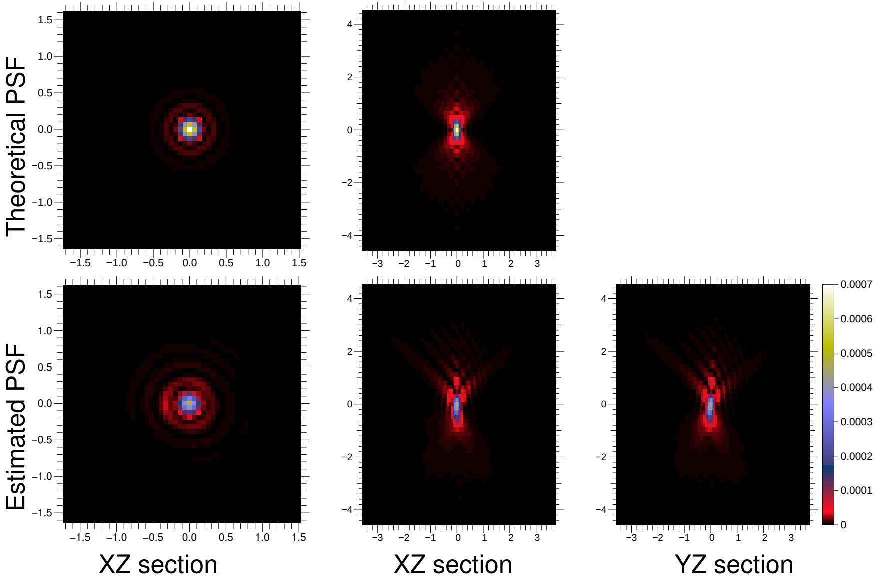


3D Radial profile of the bead

parameters	data	Hyugens	AutoDeblur	Deconvol. Lab	proposed method non-blind	proposed method blind
transversal FWHM	2.87	2.71	2.71	**2.66**	2.74	2.78
axial FWHM (in µm)	4.76	4.00	4.64	4.16	3.05	**2.98**
Relative contrast	18 %	53 %	78 %	68 %	84 %	**88** %

Performance of 3 deconvolution methods as reported by Griffa (2010) compared to the proposed method. Hyugens and AutoDeblur are commercial softwares and Deconvolution Lab is an imageJ plugin implementing (Vonesch, 2008).

Calibration bead: PSF

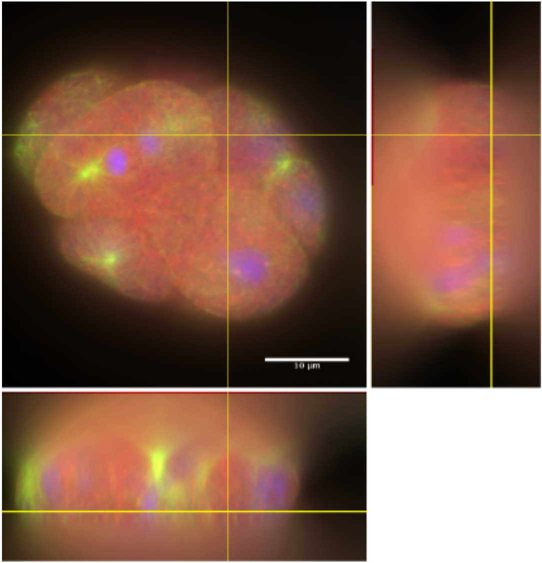


Experimental result: C. Elegans

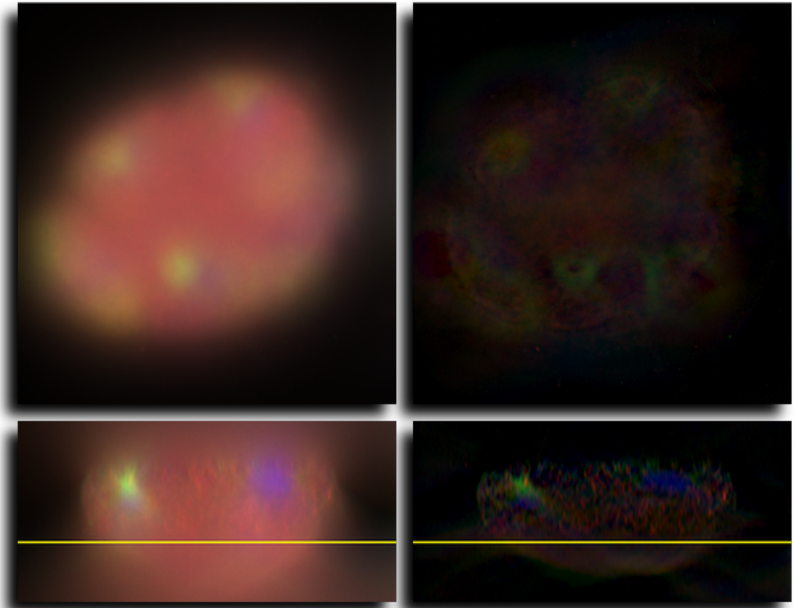
C. Elegans embryo

- $\times 63$, 1.4 NA oil objective,
- DAPI + FITC + CY3,
- $672 \times 712 \times 104$ voxels,
- voxels size $64.5 \times 64.5 \times 200\,\mathrm{nm}^3$

from *A. Griffa, N. Garin & D. Sage, G.I.T. Imaging & Microscopy, 2010.*



Experimental result: C. Elegans



Conclusion

An effective blind deconvolution method

- increase both lateral and axial resolution,
- optically motivated PSF model,
- few needed parameters (NA and wavelength),

But still one hyper-parameter to tune.

Works in progress

- extending to confocal and two photons microscopy,
- using [Denis et al 2011] for depth variant blind deconvolution.

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