Weighted-CEL0 sparse regularisation for molecule localisation in Super-Resolution microscopy with Poisson data

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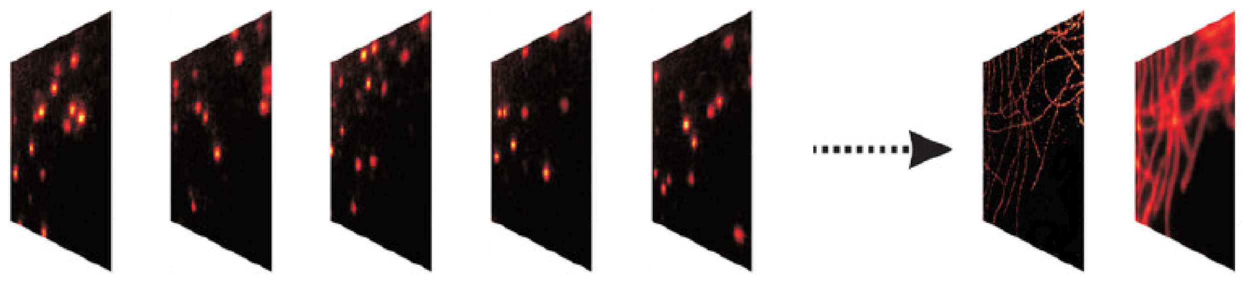
Single Molecule Localisation Microscopy

The spatial resolution of images obtained with optical microscopes is limited by **light diffraction phenomena**.



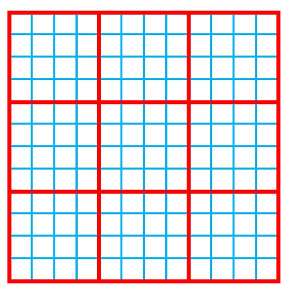
SMLM **Super-Resolution** techniques allow to overcome the diffraction barrier. The acquisition process involves fluorescent molecules, sequentially activated and deactivated at random. SMLM data consist of a **stack** of noisy blurred frames.

Acquisition Process

$\mathbf{y} \in \mathbb{R}^{M\times M}$ (coarse grid) observed image is a realisation of $\mathbf{Y} \sim Poisson(\mathbf{Ax})$ with $\mathbf{A} = \mathbf{R_L H} \in \mathbb{R}^{M^2\times N^2}$

- $\mathbf{H} \in \mathbb{R}^{N^2\times N^2}$ convolution operator (PSF)
- $\mathbf{R_L} \in \mathbb{R}^{M^2\times N^2}$ down-sampling operator

with $\mathbf{x} \in \mathbb{R}^{N\times N}$ (fine grid) with $N = LM$



Weighted-ℓ_2-ℓ_0 Variational Model

$$\mathbf{x}^* \in \underset{\mathbf{x}\in\mathbb{R}^{ML\times ML}}{\arg\min}\ G_{w\ell_0}(\mathbf{x}) := \frac{1}{2}\frac{\left((\mathbf{Ax})_j - y_j\right)^2}{y_j} + \lambda\|\mathbf{x}\|_0 + i_{\geq 0}(\mathbf{x}), \quad \lambda > 0$$

- **Fidelity** accounting for signal-dependent Poisson noise
- **Sparsity-promoting regularisation term**

ℓ_0-norm $\Longrightarrow$ non-smooth, non-continuous, non-convex, **combinatorial** and **NP-hard**. To overcome this issue, a new class of ***continuous* non-convex** penalties (**relaxations** of the ℓ_0-norm) has been studied for the ℓ_2-ℓ_0 problem.

Weighted-CEL0 relaxation

We derive a **continuous exact relaxation of $\mathbf{G}_{\mathbf{w}\ell_0}$** by computing its biconjugate functional (applying twice Fenchel conjugation):

$$G_{\mathtt{wCEL0}}(\mathbf{x}) := \frac{1}{2}\frac{\left((\mathbf{Ax})_j - y_j\right)^2}{y_j} + \Phi_{\mathtt{wCEL0}}(\mathbf{x};\lambda;\mathbf{A};\mathbf{y}) + i_{\geq 0}(\mathbf{x})$$

$G_{\mathtt{wCEL0}}$ is **non-smooth, non-convex but *continuous*** $\Longrightarrow$ the associated problem is efficiently solved algorithmically.

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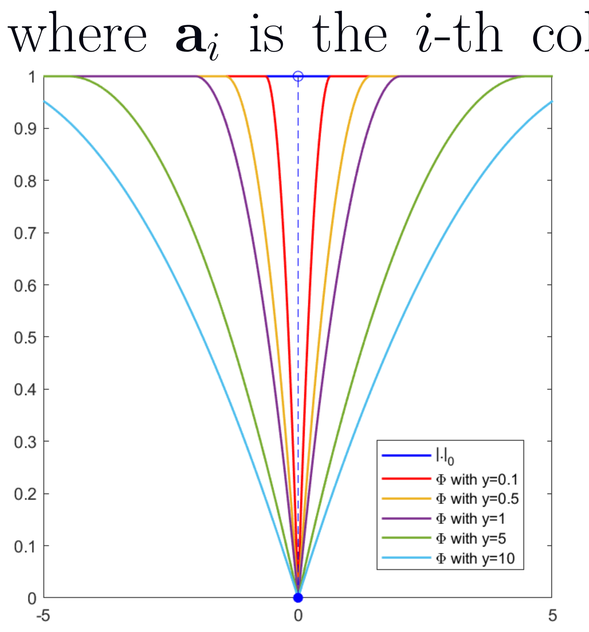
Weighted-CEL0 penalty

Non-convex non-smooth *continuous* penalty defined by:

$$\Phi_{\mathtt{wCEL0}}(\mathbf{x};\lambda;\mathbf{A};\mathbf{y}) := \sum_{i=1}^{N^2} \lambda - \frac{\|\tilde{\mathbf{a}}_i\|^2}{2}\left(|x_i| - \frac{\sqrt{2\lambda}}{\|\tilde{\mathbf{a}}_i\|}\right)^2 \mathbb{1}_{\{|x_i| < \frac{\sqrt{2\lambda}}{\|\tilde{\mathbf{a}}_i\|}\}}$$

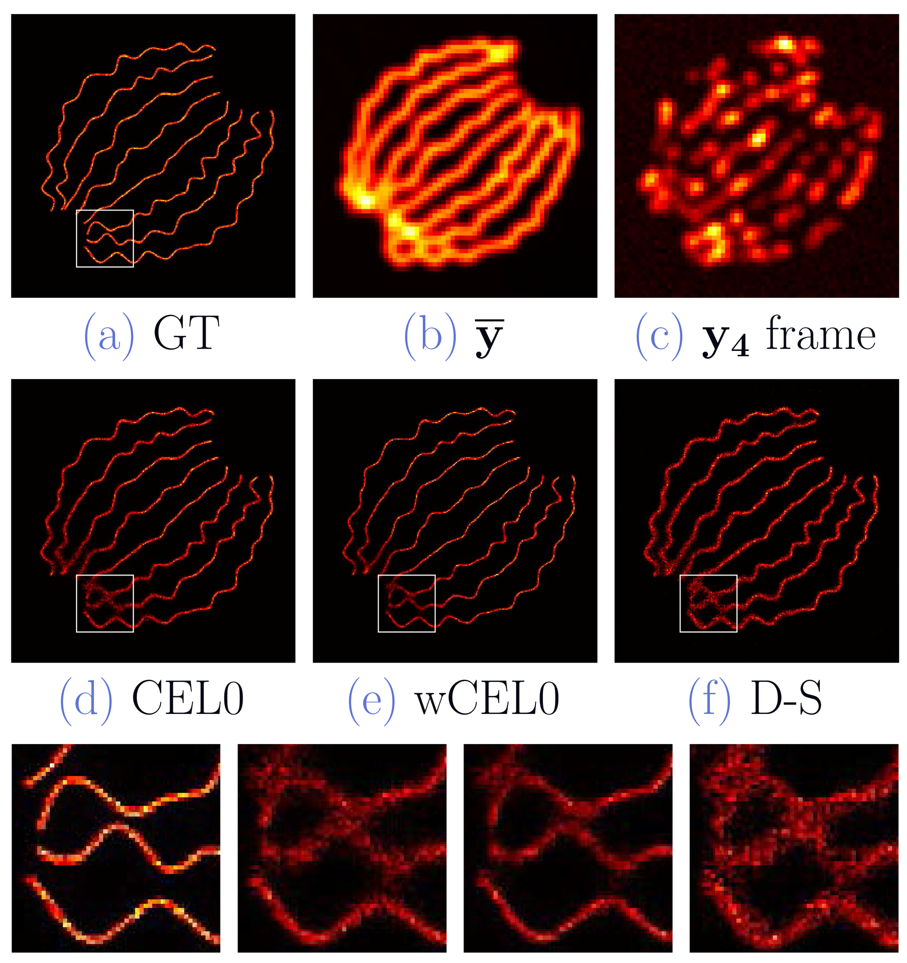
where $\mathbf{a}_i$ is the i-th column of the matrix $\mathbf{A}$ and $\tilde{\mathbf{a}}_i := \mathbf{a}_i./\mathbf{y}$.



Compared to the $\Phi_{\mathtt{CEL0}}$ penalty for the standard $\ell_2 - \ell_0$ problem, the new penalty $\Phi_{\mathtt{wCEL0}}$ presents an explicit dependence on both the model (i.e. the columns of the operator $\mathbf{A}$, as for CEL0) and the data $\mathbf{y}$, reflecting the **intrinsic signal-dependence** encoded into the considered Poisson modelling.

Numerical Results

High-density ISBI SMLM 2013 dataset: 361 frames stack



(a) GT (b) $\bar{\mathbf{y}}$ (c) $\mathbf{y}_4$ frame
(d) CEL0 (e) wCEL0 (f) D-S
(g) GT (h) CEL0 (i) wCEL0 (j) D-S

- N=256, M=64, L=4
- Gaussian PSF, FWHM = 258.2nm

We compare the proposed wCEL0 method with the previous CEL0 method (which describes Additive Gaussian White Noise) and Deep-STORM, a deep-learning based model for super-resolution microscopy.

1st-row: (a) ground truth, (b) sum of all the acquisitions, (c) 4th acquired frame. **2nd row**: (d) CEL0 result, (e) wCEL0 result, (f) Deep-STORM result. **3rd row**: close-up on a detail.

	J_0	J_2	J_4	CD	FN	FP
CEL0	0.042	0.467	0.552	121	96	**3**
wCEL0	**0.057**	**0.552**	**0.659**	151	67	14
Deep-STORM	0.025	0.037	0.038	**217**	**1**	8157

Table: Number of Correctly Detected molecules CD, False Negatives FN, False Positives FP for tolerance radius $\delta = 4$. Jaccard index $J_\delta \in [0,1]$ up to tolerance radius $\delta \in \{0,2,4\}$, computed as mean over the frames. $J_\delta \in [0,1]$ is the ratio between CD and the sum of CD, FN and FP.

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