

**Title:** *On some reconstruction problems in MA-TIRF imaging and sparse optimization using continuous exact relaxation of  $\ell_0$ -penalized criteria.*

**Abstract:** This thesis is devoted to two problems encountered in signal and image processing: 3D reconstruction for multi-angle total internal reflection fluorescence microscopy (MA-TIRF) and sparse optimization via  $\ell_2$ - $\ell_0$  minimization.

MA-TIRF microscopy is a method of choice to observe subcellular biological processes. It proceeds by acquiring a set of 2D images using tilted laser beams in the total internal reflection regime. Then, the resolution of an ill-posed inverse problem gives access to a super-resolution information on the axial position of the observed biological structures. We proposed to tackle this problem by deploying a numerical solution which performs jointly the estimation of the fluorophore density and the estimation of the background signal. In particular, we showed that considering this background signal in the reconstruction process is crucial in order to avoid significant errors on the reconstructed volume. On the other hand, handling real data requires an accurate calibration of the system. From acquisitions of the back focal plane of the objective, we proposed a method to numerically adjust the model that links the incident angle to some system parameters. Then, in order to validate the reconstruction method, we deployed different experiments based on samples with known geometry. The proposed method has been shown to be able to reconstruct precisely such samples on a 400 nm depth layer with an axial resolution of 20 nm. These results were corroborated with a co-localization experiment of two fluorescent molecules (sensitive to different excitation wavelengths) used to stain the same biological structures. Finally, the proposed reconstruction method has been used to the study of the cell adhesion process. The obtained reconstructions have allowed to observe biological phenomena confirming previous experiments for which a quantitative measure of the axial position of the biological structures was not available.

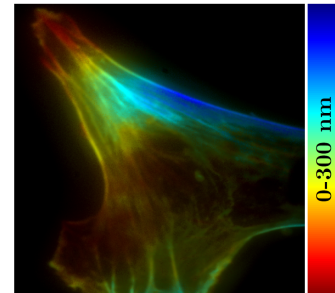


Figure 1: Reconstruction of actin filaments (the color code represents the axial position).

The second part of this thesis concerns the  $\ell_0$ -regularized least-squares minimization problem

$$\hat{x} \in \left\{ \arg \min_{x \in \mathbb{R}^N} G_{\ell_0}(x) := \frac{1}{2} \|\mathbf{A}x - \mathbf{y}\|_2^2 + \lambda \|x\|_0 \right\}, \quad (1)$$

where  $\mathbf{A} \in \mathbb{R}^{M \times N}$  is a linear operator,  $\mathbf{y} \in \mathbb{R}^M$  is a data vector,  $\|\cdot\|_0$  is the  $\ell_0$  pseudo-norm, and  $\lambda > 0$  is a regularization parameter. We proposed a study of continuous relaxations  $\tilde{G}(x) := \frac{1}{2} \|\mathbf{A}x - \mathbf{y}\|_2^2 + \Phi(x)$ , which are equivalent to the initial functional  $G_{\ell_0}$  in terms of minimizers. More precisely, we exhibited penalties  $\Phi$  such that the two following properties are satisfied

$$\arg \min_{x \in \mathbb{R}^N} \tilde{G}(x) = \arg \min_{x \in \mathbb{R}^N} G_{\ell_0}(x) \quad (P1)$$

$$\hat{x} \text{ (local) minimizer of } \tilde{G} \Rightarrow \hat{x} \text{ (local) minimizer of } G_{\ell_0}. \quad (P2)$$

The penalties  $\Phi$  leading to relaxations  $\tilde{G}$  with these properties are said to be *exact*. It is worth noting that for (P2), the converse is not imposed. Hence,  $\tilde{G}$  can eliminate some local (non-global) minimizers of  $G_{\ell_0}$ . This is an interesting property in this difficult context of non-convex optimization.

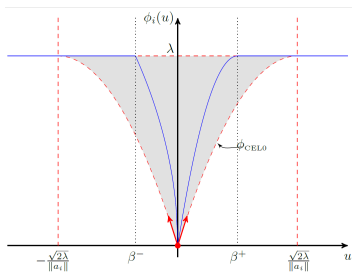


Figure 2: Illustration of the necessary and sufficient conditions (in red) that ensure  $\{(P1), (P2)\}$ . An example of penalty verifying the conditions is drawn in blue.

Starting from the computation of the convex hull of  $G_{\ell_0}$  when the columns of  $\mathbf{A}$  are orthogonal, we proposed the Continuous Exact  $\ell_0$  (CEL0) penalty. Although the resulting relaxation  $G_{\text{CEL0}}$  is not anymore the convex hull of  $G_{\ell_0}$  for an arbitrary matrix  $\mathbf{A} \in \mathbb{R}^{M \times N}$ , we showed that properties (P1) and (P2) are satisfied and that some local (non-global) minimizers of  $G_{\ell_0}$  are eliminated by  $G_{\text{CEL0}}$ . Within a unifying approach, we then studied a class of exact penalties leading to relaxations  $\tilde{G}$  verifying the properties (P1) and (P2). We considered separable penalties  $\Phi(x) = \sum_i \phi_i(x)$  and derived *necessary and sufficient* conditions on the  $\phi_i$  which ensure that the associated relaxation  $\tilde{G}$  is exact. We get back the CEL0 penalty as the inferior limit of the derived class of penalties. These conditions provide a new vision of relaxations of the  $\ell_0$  pseudo-norm by allowing their comparison from the perspective of properties (P1) and (P2). For instance we showed that, with a judicious choice of the parameters of some state-of-the-art penalties, the resulting relaxation  $\tilde{G}$  satisfies properties (P1) and (P2). Among them, we showed that the CEL0 relaxation was eliminating the larger amount of local (non-global) minimizers of  $G_{\ell_0}$ . Finally, we used these relaxations for various applications in signal and image processing.