



# Multi-scale Graph-based Guided Filter for De-noising Cryo-Electron Tomographic Data (MG<sup>2</sup>F)

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## Overview and Motivation

Cryo-electron tomography (CET) is a powerful imaging technique in biological sciences which bridges the gap between the molecular and the cellular structural biology [5], giving a better understanding of protein interactions and thus better drug delivery strategies. In principle, similar to Computed Tomography (CT) in Medical Imaging, the acquired projections at limited angles are reconstructed back to create the 3D object, however, these projections are extremely noisy and have a low contrast. Therefore, many conventional filters failed in smoothing the background while preserving edges and interesting objects, which makes developing a denoising algorithm is very desirable for better interpretation.

### Contributions:

- By Using a multi-scale pyramid for guidance we are able to detect meaningful scales and use them for guidance without over-smoothing fine scale structures.
- Using a patch-based approach, we can take advantage of redundant structures in the whole image rather than using a pre-defined spatial window for averaging similar pixels or patches. This way, we can preserve the local and global consistencies.
- By Deriving explicit solution formulas for computing the intermediate filtering results we obtain an efficient algorithm.

## Methodology & MG<sup>2</sup>F Algorithm:

Given a noisy image  $I_\eta$ , we collect  $N$  overlapping patches, which can be seen as data points  $v = \{v_1, v_2, \dots, v_N\} \in \mathbb{R}^{n \times N}$  lying on a manifold  $\mathcal{M}$  embedded in  $\mathbb{R}^n$  space such that  $v = EI_\eta$ , where  $E$  is an operator collecting patches and vectorize it, cf. Figure 1. The relation between the data points can be represented by a k-NN connected, undirected, and weighted graph  $G = \{v, \varepsilon, \omega\}$ , where  $\varepsilon$  is the set of edges, and  $\omega$  is the set of edge weights.

These weights are assigned using a heat kernel, however, the distance between these patches is computed on a certain structure scale  $\sigma_s$  where the noise manifest itself and can be used as a guidance for the graph spectral filter  $h(\lambda_i)$ , which is computed based on the eigenvalue decomposition of the normalized Laplacian matrix  $\tilde{L}_{\sigma_s} := U\Lambda U^T$ . This way, we can formulate the denoising problem as follows:

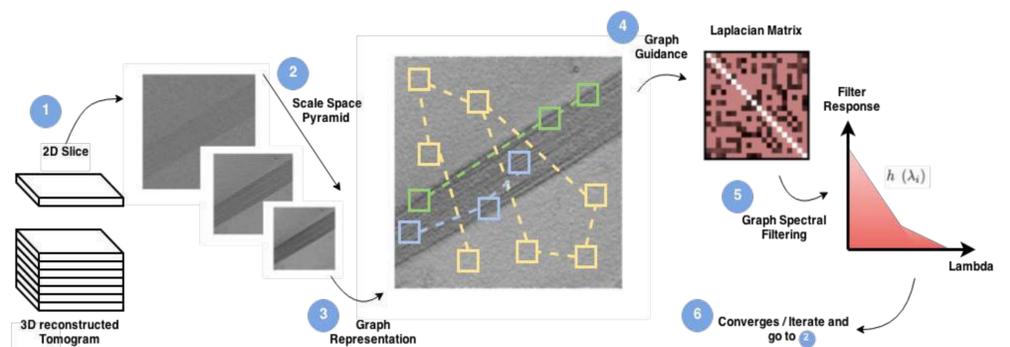
$$\hat{I}_f = \arg \min_{I_f} \left\{ \frac{1}{2} \|I_f - I_\eta\|_2^2 + \alpha S_{\sigma_s}(I_f) \right\},$$

where  $\alpha > 0$  is the regularization parameter and  $S_{\sigma_s}(I_f) = \frac{1}{2} \text{Tr}(vL_{\sigma_s}v^T)$  is the graph guidance regularization term.

The closed form solution can be written as

$$\hat{I}_f = E^T \left( \sum_{i=1}^N \frac{1}{(1 + \alpha \lambda_i)} u_i \hat{v}_i \right) = E^T \left( \frac{1}{I + \alpha \tilde{L}_{\sigma_s}} \right) EI_\eta,$$

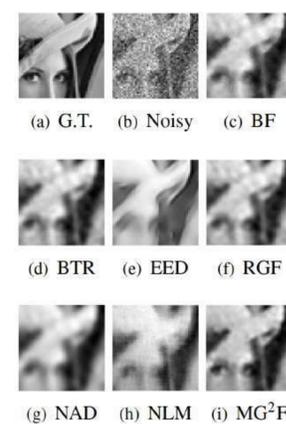
where  $E^T$  denotes the reshaping process of the previously vectorized patches, and the spectral response of the filter  $h(\lambda_i) = 1/(1 + \alpha \lambda_i)$  controls the frequency decay and thus the degree of smoothness. A connection to classical filters and the sensitivity analysis are discussed in details.



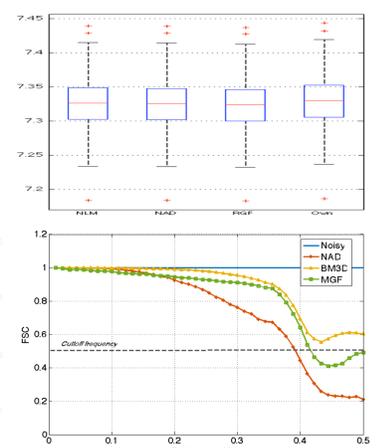
**Figure 1: MG<sup>2</sup>F Framework:** A noisy image slice from the 3D reconstructed tomogram is fed to the algorithm, where the graph is built on a selected scale space image (i.e. coarse grid) acting as a guidance for the regularized graph spectral filter.

## Experiments & Results:

### Photographic Image:

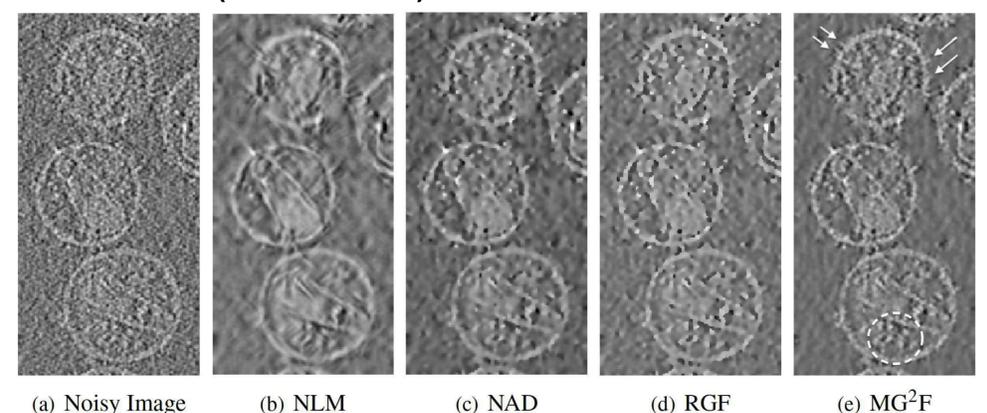


Algorithm Parameters	PSNR (dB)
Bilateral (BF) [7] ( $\sigma_r=0.5, \sigma_g=1.5, W=10$ )	17.49
Beltrami (BTR) [2] ( $\delta=0.1, iter=10$ )	17.37
EED [6] ( $\rho=4, iter=30$ )	11.27
NAD [4] ( $iter=10, \kappa=0.3$ )	16.50
NLM [1] ( $P=7, W=21, \sigma_s=4\sigma_n$ )	12.11
RGF [3] ( $\sigma_r=0.5, \sigma_g=1.5, iter=10$ )	17.49
MG <sup>2</sup> F ( $\alpha=0.8, iter=4, \sigma_s=0.1$ )	<b>17.78</b>

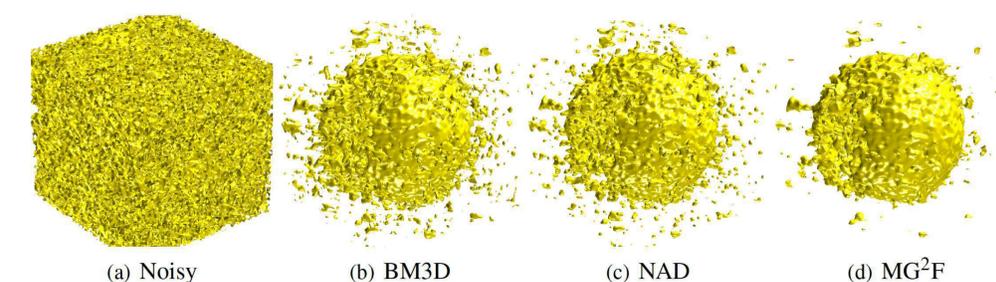


**Left:** Filtering results on Lena Image compared with different methods, **Top right:** PSNR box plot on 100 simulated 2D CET data (SNR: 0.1dB), **Bottom right:** The Fourier Shell Correlation of 3D CET data.

### Real CET data (EMDB-ID:1155):



**2D CET data:** Filtering results on the tomogram along with the corresponding CNR of b) NLM (0.1979), c) NAD (0.2570), d) RGF (0.3146), e) Proposed MG<sup>2</sup>F (**0.3150**), where the arrows point to the fine structures on the membrane and the ellipse contains the inner core of HIV virus.



**3D CET Data:** A comparison between different 3D filtering methods to our proposed MG<sup>2</sup>F method on real unstained HIV-1 data (EMDB-ID: 1155).

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