MULTIFRAME SURE-LET DENOISING OF TIMELAPSE FLUORESCENCE MICROSCOPY IMAGES

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Abstract

Due to the random nature of photon emission and the various internal noise sources of the detectors, real timelapse fluorescence microscopy images are usually modeled as the sum of a Poisson process plus some Gaussian white noise. In this paper, we propose an adaptation of our SURE-LET denoising strategy to take advantage of the potentially strong similarities between adjacent frames of the observed image sequence. To stabilize the noise variance, we first apply the generalized Anscombe transform using suitable parameters automatically estimated from the observed data. With the proposed algorithm, we show that, in a reasonable computation time, real fluorescence timelapse microscopy images can be denoised with higher quality than conventional algorithms.

Observation Model

- **In the image domain:**

$y = \alpha s + b$ where $\begin{cases} s \sim \mathcal{P}(x) : \text{Poisson process with intensity } x \\ b \sim \mathcal{N}(\mu, \sigma^2) : \text{AGWN with mean } \mu \text{ and variance } \sigma^2 \end{cases}$

- **After the generalized Anscombe transform (GAT):**

$\mathcal{A}(y) = \frac{2}{\alpha}\sqrt{\alpha y + \frac{3}{8}\alpha^2 + \sigma^2 - \alpha\mu}$ and then $\mathcal{A}(y) \sim \mathcal{N}(\mathcal{A}(\alpha x + \mu), 1)$

$\Longrightarrow$ standard additive Gaussian white noise (AGWN)

Parameters Estimation

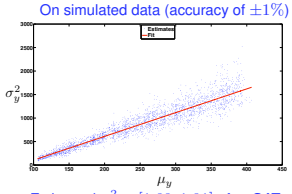
- **Reliable estimation of the parameters involved in the observation model:**

$$\left.\begin{array}{rcl} \mu_y \overset{\text{def}}{=} & \mathscr{E}\{y\} & = \alpha x + \mu \\ \sigma_y^2 \overset{\text{def}}{=} & \text{Var}\{y\} & = \alpha^2 x + \sigma^2 \end{array}\right\} \Longleftrightarrow \sigma_y^2 = \alpha\mu_y + \underbrace{\sigma^2 - \alpha\mu}_{\beta}$$

Simple procedure:

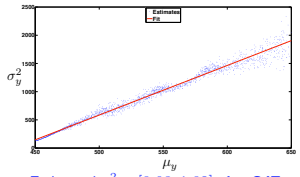
1. Compute the variance and the mean in many flat regions of the noisy image sequence to estimate σ_y^2 and μ_y.
2. Perform a robust linear regression on the set of points (μ_y, σ_y^2).
3. Identify α as the slope of the fitted line and β as the intercept at $\mu_y = 0$.

On simulated data (accuracy of $\pm 1\%$)



Estimated $\sigma^2 \in [1.00, 1.01]$ after GAT

On real data



Estimated $\sigma^2 \in [0.98, 1.02]$ after GAT

Multiframe SURE-LET

- **Notation:** sequence of C N-pixels images

$\mathbf{x} = [\mathbf{x}_1, \mathbf{x}_2, \ldots, \mathbf{x}_N]$ where $\mathbf{x}_n = [x_{n,1}, x_{n,2}, \ldots, x_{n,C}]^{\mathrm{T}}$

- **Noisy sequence model after GAT:**

$\mathbf{y} = \mathbf{x} + \mathbf{b}$, where each $\mathbf{b}_n \sim \mathcal{N}(\mathbf{0}, \mathbf{R})$

- **Two key ingredients:**
  - **Multiframe *Stein's unbiased risk* (mean-squared error) *estimate* (SURE):**

$$\epsilon = \frac{1}{CN}\sum_{n=1}^{N} \|\boldsymbol{\theta}(\mathbf{y}_n, \mathbf{p}_n) - \mathbf{y}_n\|^2 + \frac{2}{CN}\sum_{n=1}^{N} \text{Tr}\left\{\nabla_{\mathbf{y}_n} \mathbf{R}^{\mathrm{T}} \boldsymbol{\theta}(\mathbf{y}_n, \mathbf{p}_n)\right\} - \frac{1}{C}\text{Tr}\{\mathbf{R}\}$$

$\hat{\mathbf{x}}_n = \boldsymbol{\theta}(\mathbf{y}_n, \mathbf{p}_n)$: multiframe estimation of $\mathbf{x}_n$.

$\mathbf{p}_n$: independent of $\mathbf{y}_n$, e.g. parent built out of the group delay compensated (GDC) lowpass subband at same scale in orthonormal wavelet transform (OWT).

  - **Multiframe *linear expansion of thresholds* (LET):**

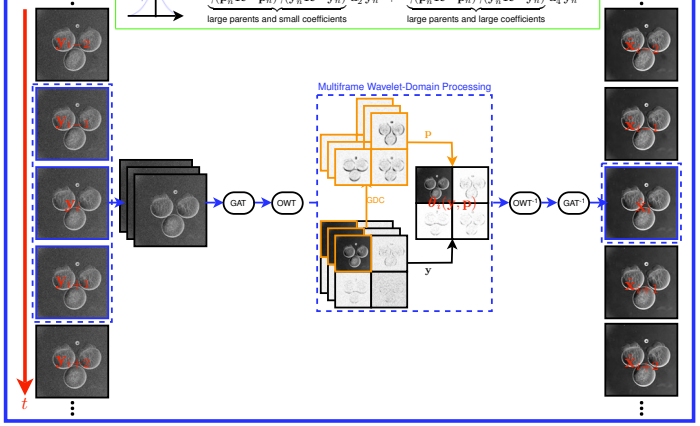
$$\boldsymbol{\theta}(\mathbf{y}_n, \mathbf{p}_n) = \sum_{k=1}^{K} \mathbf{a}_k^T \boldsymbol{\theta}_k(\mathbf{y}_n, \mathbf{p}_n)$$

- **Parameters optimization by SURE minimization:**

SURE+LET $\Longleftrightarrow$ $\mathbf{a}_{\text{opt}}$ solution of a linear system of equations

Algorithm

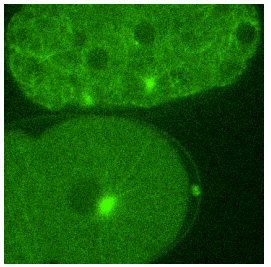
$$\boldsymbol{\theta}(\mathbf{y}_n, \mathbf{p}_n) = \underbrace{\gamma(\mathbf{p}_n^{\mathrm{T}}\mathbf{R}^{-1}\mathbf{p}_n)\gamma(\mathbf{y}_n^{\mathrm{T}}\mathbf{R}^{-1}\mathbf{y}_n)}_{\text{small parents and small coefficients}}\mathbf{a}_1^{\mathrm{T}}\mathbf{y}_n + \underbrace{\overline{\gamma}(\mathbf{p}_n^{\mathrm{T}}\mathbf{R}^{-1}\mathbf{p}_n)\gamma(\mathbf{y}_n^{\mathrm{T}}\mathbf{R}^{-1}\mathbf{y}_n)}_{\text{large parents and small coefficients}}\mathbf{a}_2^{\mathrm{T}}\mathbf{y}_n + \underbrace{\overline{\gamma}(\mathbf{p}_n^{\mathrm{T}}\mathbf{R}^{-1}\mathbf{p}_n)\gamma(\mathbf{y}_n^{\mathrm{T}}\mathbf{R}^{-1}\mathbf{y}_n)}_{\text{large parents and small coefficients}}\mathbf{a}_3^{\mathrm{T}}\mathbf{y}_n + \underbrace{\overline{\gamma}(\mathbf{p}_n^{\mathrm{T}}\mathbf{R}^{-1}\mathbf{p}_n)\overline{\gamma}(\mathbf{y}_n^{\mathrm{T}}\mathbf{R}^{-1}\mathbf{y}_n)}_{\text{large parents and large coefficients}}\mathbf{a}_4^{\mathrm{T}}\mathbf{y}_n$$



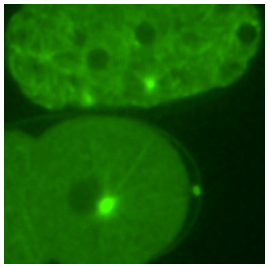
Experiments on Real Data

- **Timelapse fluorescence microscopy image sequence of C. Elegans embryos:**
  - **Material:** Olympus IX81 motorized inverted microscope with spinning disk.
  - **Acquisition process:** 1000 frames imaged at 2 Hz.
  - **Biological context:** green fluorescent protein (GFP) tags tubulin molecules in the embryos during their cellular division.

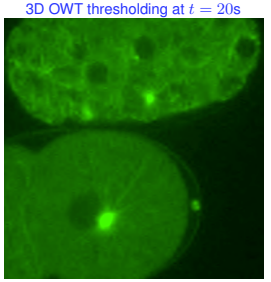
Raw data at $t = 20$s



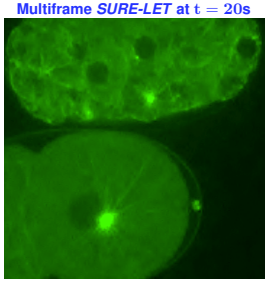
3D Median filter at $t = 20$s



3D OWT thresholding at $t = 20$s

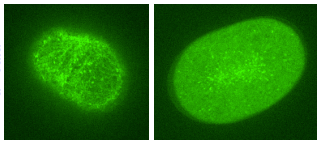


Multiframe *SURE-LET* at t = 20s

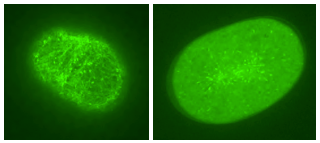


- **More denoising results:**

Raw data



Denoised data



Conclusion

- **Valid observation model** for most fluorescence microscopy images.
- Adjacent frames correlations efficiently integrated thanks to a fully data-adaptive **Multi-frame wavelet-domain** denoising .
- **High quality** denoising achievable in a **reasonable computation time** ($\sim$1.5s to process a 512×512 frame).

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