



## Microarray image enhancement techniques by denoising: Current status and future directions

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### ABSTRACT

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Microarray imaging is a technique for simultaneously detecting the expression of numerous genes. Microarrays are simply a slide with unique Deoxyribonucleic Acid (DNA) probes, often known as gene chips. This paper aims to provide an overview of important contributions to the field of image denoising in the context of microarray imaging. The methodologies discussed in the article include various techniques of transform domain and spatial filtering methods for denoising microarray images that can be used to improve the quality of microarray images. We have identified the strengths and limitations of these techniques and highlights their potential impact. The paper also explores future developments in this area and discusses their potential impact, on microarray imaging.

**Contribution/Originality:** This study contributes to the existing literature review. It summarizes the body of knowledge on microarray image enhancement methods in a thorough and organized manner, pointing out gaps and potential research directions. Include a summary of the various microarray image denoising and performance testing metrics. This study also proposes an idea based on the existing literature analysis to combine Gaussian and Poisson noise models to capture both background noise and noise brought on by low-level expression levels.

## 1. INTRODUCTION

### 1.1. Digital Images and Noise

With the massive creation of digital photographs and films taken in bad settings, the demand for image improvement and restoration approaches has risen. Regardless of camera quality, image augmentation is always desirable to broaden the range of motion. Unlike a normal photograph, a digital image [1] is made up of small individual locations of a certain color or a certain level of grayscale intensity. Images are stored in memory basically as a very long list of numbers and along with other information about the width and height of the image. These pixels are accessed to determine their color and to perform certain operations like applying filters or compiling them into a video. The real values in 2D dimensions are represented by the points on the grayscale image. A pixel in a color image, on the other hand, is a triplet of Red (R), Green (G) and Blue (B) values. To simplify the notation and presentation of the experiment, we will limit our work to rectangular 2D grayscale images.

Blur and noise are the two most typical image accuracy limitations. The finite number of samples are there in blurred digital images, the number of samples has to satisfy Shannon Nyquist's sampling criterion, and blur is specific to imaging systems [2]. Noise is the second significant visual detriment [3]. To determine the result of light intensity for each pixel value  $u(i)$ , Charge Coupled Device (CCD) matrix and a light focusing device are

frequently utilized. The number of incoming photons is used for a predetermined amount of time corresponding to the obturation duration in each CCD quadrant, typically a square. The central limit theorem states that when the source of light remains constant, the fluctuation of the number of photons in each pixel is about the average number. In other words, for an incoming photon, one can anticipate fluctuations of order  $n$ .

Furthermore, each captor acquires heat spurious photons if it isn't adequately cooled. The ensuing disturbance is commonly referred to as "obscurity noise." One can write a first approximate estimate as follows:

$$v(i) = u(i) + n(i)$$

Were,  $I \in I$

$v(i)$  - Observed value.

$u(i)$  - "actual" value at pixel  $I$ .

$n(i)$  - Noise disturbance.

As previously stated, the quantity of noise is signal dependent, i.e., when  $u(i)$  is greater,  $n(i)$  is greater. In noise models, it is assumed that the normalized values of  $n(i)$  and  $n(j)$  at different pixels are independent random variables, and this is referred to as white noise.

### 1.2. Microarray Image

Gene sequencing and gene expression research on a big scale, complementary Deoxyribonucleic Acid (cDNA) [4] microarray imaging is a valuable tool and strong technology. DNA microarrays are a technical convergence of biology and computers that allows for genome-wide gene expression analysis in humans. Millions of gene-specific probes are usually grouped in a tiny grid like: Labeled nucleic acids derived from tissue type, developmental level, or other state of interest are probed on a glass slide or microchip, as well as this matrix. As a result, thousands of genes' expression profiles can be analyzed at the same time under those conditions [5]. This method, in particular, is now widely regarded as a valuable tool for researching the genetic underpinnings of complicated disorders.

The development of this imaging approach over the last decade was motivated by Southern research in the 1970s [6]. Thousands of genes are synthesized on a single slide in microarray research, and all genes can be examined at the same time. This allows for systematic and thorough DNA and Ribonucleic Acid (RNA) variation study [7] molecular biology research, and genetic medical assessment, like detection of cancer Leyten, et al. [8] and Sun, et al. [9] types 1 and 2. It's a common diabetes treatment [10] and Diagnosis.

The slide shows the DNA sequence. Gene expression data can be generated after additional image processing for additional studies like gene grouping and detection. Analysis of cluster can be used to find genes that are controlled in comparable ways in different situations. DNA grids could also be used to distinguish between cell types in various tissues, such as: Healthy cells against cancer cells, tumors that react differently, or control cells versus drug-treated cells. DNA sequences can be seen on the slides. After additional picture processing, gene expression data can be generated for more investigation, including gene clustering or recognition. Cluster analysis can be used to identify genes which are regulated in a similar fashion in a range of circumstances. DNA arrays can also be utilized to distinguish between normal cells and cancer cells, tumors with varied treatment responses, and control cells versus treated cells with a specific drug across different tissue types.

## 2. CLASSIFICATION OF DENOISING ALGORITHMS

The image denoising techniques are mainly categorized into two classes: Transform domain and spatial filtering methods, as shown in Figure 1.

### 2.1. Spatial Filtering

Using spatial filters is a common method for removing noise from visual data. There are two categories of spatial filters: linear and non-linear.

### 2.1.1. Non-Linear Filters

Nonlinear filters are not identified noises directly and reduce them. Spatial filters are nonlinear filters it applies a low pass filtering technique on image pixels by assuming the detection of noise occurs in a higher frequency spectrum. The spatial filters eliminates noise to an acceptable rate but create blurriness at the edges of objects in images. These problems are addressed in recent research, and the nonlinear median type filters achieve a better noise reduction rate. Some of the nonlinear median filters are; relaxed median [11] rank conditioned rank selection [12] and weighted median filters [13].

### 2.1.2. Linear Filters

The mean filters reduce the best-fitted gaussian distribution effectively concerning mean square error. The sharp edges are smeared, outlines, and other fine visual elements, are destroyed, and linear filter efficiency is impaired with the existence of signal-dependent noise. If the underlying noise signal is smooth and requires knowledge of noise and original signal spectrum, the Wiener filtering approaches [14] are best fitted and achieve the best efficiency. Controlling model complexity is similar to window size selection in the Wiener technique, which uses spatial smoothing. The drawbacks of Wiener filtering have been addressed by developing wavelet-based denoising techniques [14-17].

## 2.2. Transform Domain Filtering

Based on the basis functions utilized, transformation domain filtering techniques can be divided into several groups. Primitives can be either adaptive or non-adaptive to data. Non-adaptive changes are addressed first since they are more typical.

### 2.2.1. Spatial-Frequency Filtering

In spatial frequency filtering, low-pass filters with the Fast Fourier Transform (FFT) are employed. If the noise component is uncorrelated from the signals available in the frequency domain, the frequency smoothing approach [18] creates a frequency domain filter and adjusts the cutoff frequency to eliminate noise. These approaches are costlier in terms of time, and depend on the cutoff frequency and the behavior of the filter. Also, the frequency of the processed image may be incorrect.

### 2.2.2. Wavelet Domain

There are two categories of filtering operations in the wavelet domain: linear and nonlinear.

#### 2.2.2.1. Linear Filters

If signal corruption is described as a Gaussian process and the accuracy requirement is mean squared error (MSE), a linear filter of the wavelet domain (e.g., B. Wiener filter, best result) [19]. The filtering process reduced the MSE. Even in this scenario, using a detection method based on this hypothesis almost always results in a median filter which is visually worse than the initial noisy signal. [Mastriani and Giraldez \[20\]](#) is used to denoise the image. It includes a wavelet domain Wiener filter method that only conducts Wiener filtering inside each level and does not allow filtering between scales.

#### 2.2.2.2. Non-Linear Threshold Filtering

Non-linear coefficient thresholding is used in the most extensively studied techniques for Wavelet Transform denoising. The method takes advantage of the wavelet transform's sparsity as well as the fact that it translates signal domain white noise to transform domain white noise. As a result, although signals potential in the transform

domain concentrates into fewer coefficients, noise energy does not. Signal and noise can be differentiated using this fundamental idea.

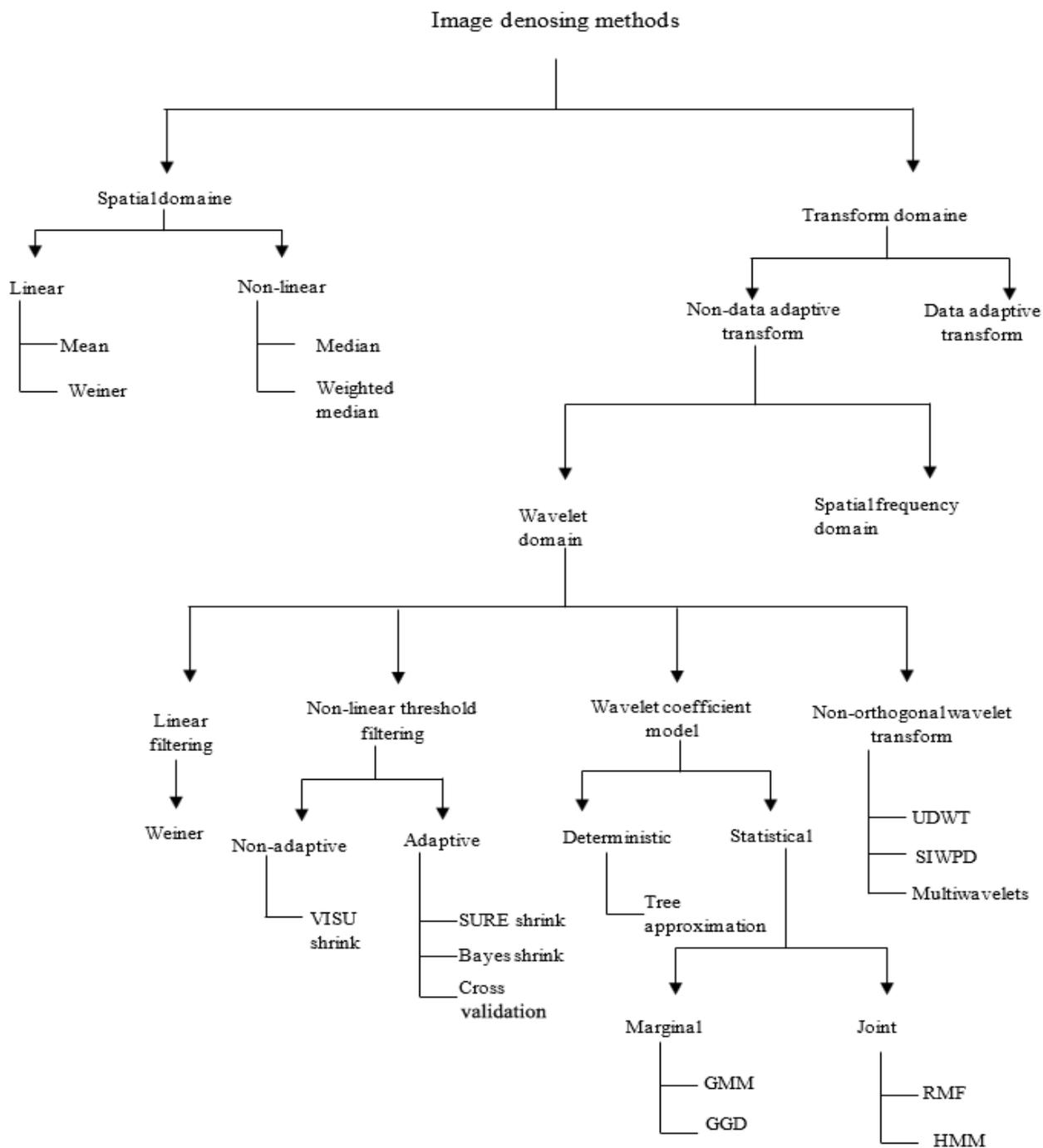


Figure 1. Various types of image denoising techniques.

Note: UDWT: Undecimated discrete wavelet transform, SIWPD: Speech impairment with word prediction and Dyslexia, GMM: Gaussian mixture model, GGD: Generalized gaussian distribution, RMF: Random matrix framework, HMM: Hidden Markov model.

Hard Thresholding [21, 22] is a process where, minor coefficients are neglected and rest are considered. However, as a result of unsuccessful attempts to remove fairly significant noise coefficients, the method produces artificial blips, also known as artefacts, in the photographs. Wavelet transform with soft thresholding was also presented in Jing-yi, et al. [21] to solve the drawbacks of hard thresholding. Coefficients exceeding the threshold are shrunk by the threshold's absolute value in this technique. Semi-soft thresholding and Garrote thresholding are two alternative strategies for applying thresholds that are similar to soft thresholding [23]. The main topic of wavelet shrinkage research is how to choose the appropriate threshold, which may be adaptive or non-adaptive.

### a. *Non-Adaptive Thresholds*

The VISUShrink [24] is based solely on the quantity of data points. It possesses asymptotic equivalence, implying that as the number of pixels reaches infinite, it performs best in terms of MSE. VISUShrink is known for producing overly smoothed images based on the number of pixels in input image, which causes its threshold decision to be unreasonably huge.

### b. *Adaptive Thresholds*

SUREShrink [20] outperforms VISUShrink by combining the SURE and universal threshold criterion. BayesShrink [25, 26] uses a Generalized Gaussian prior to minimize the Bayes' Risk Estimator function, resulting in a data adaptive threshold. Most of the time, BayesShrink outpaces SUREShrink [27].

When noise levels approach signal magnitudes, we can consider the hypothesis that the distinguish between noise and co-efficient magnitude of signal are broken. The spatial arrangement of nearby wavelet coefficients may be essential for locating noisy signals in this high noise environment. Important characteristics (such straight lines and curves) are frequently produced by signals, whereas noisy coefficients are randomly distributed.

#### 2.2.2.3. *Non-orthogonal Wavelet Transforms*

To obtain a visually better solution, the signal was decomposed using the Undecimated Wavelet Transform (UDWT). Because UDWT is shift invariant, it removes visual artefacts like the pseudo-Gibbs effect. Using UDWT adds a significant amount of computational cost, making it less feasible, even though the improvement in outcomes is far bigger. In addition to UDWT, Multiwavelets are being researched, which enhances performance but adds to the processing complexity. On a single dataset, multiwavelets are created by combining different mother functions (scaling functions). The authors of Peng, et al. [28] tackle a problem by combining shift invariance and Multiwavelets.

#### 2.2.2.4. *Wavelet Coefficient Model*

The multiresolution properties of the Wavelet Transform are used in this method. This method detects strong signal correlation at several resolutions by evaluating the signal at multiple resolutions. This approach delivers good results, but it is significantly more computationally demanding and expensive.

##### 2.2.2.4.1. *Deterministic*

A tree structure of wavelet coefficients is generated using the Deterministic modelling technique, with each level representing a transformation scale and nodes representing wavelet coefficients. Sadeghigol, et al. [29] employs this method. The optimal tree approximation is used to interpret wavelet decomposition hierarchically. The singular wavelet coefficient has a large wavelet coefficient that remains along the branch. When there is a signal in the wavelet coefficient, it should have a higher presence at its parent nodes if it is important at one node.

##### 2.2.2.4.2. *Statistical Wavelet Coefficient Modeling*

The Wavelet Transform's characteristics are made use of by the Statistical Wavelet Coefficient Modeling method to enhance the modelling of visual data. The multiscale correlation between wavelet coefficients and the local correlation between neighbourhood coefficients are the two main aspects of the Wavelet Transform that are the emphasis of this technique. A thorough review of the statistical properties of wavelet coefficients is given by Lyashenko, et al. [30]. The method uses joint and marginal probabilistic models, which are built on a probabilistic model, to take advantage of these characteristics. The performance of the method as a whole is enhanced by these models' assistance in correctly simulating the statistical characteristics of wavelet coefficients.

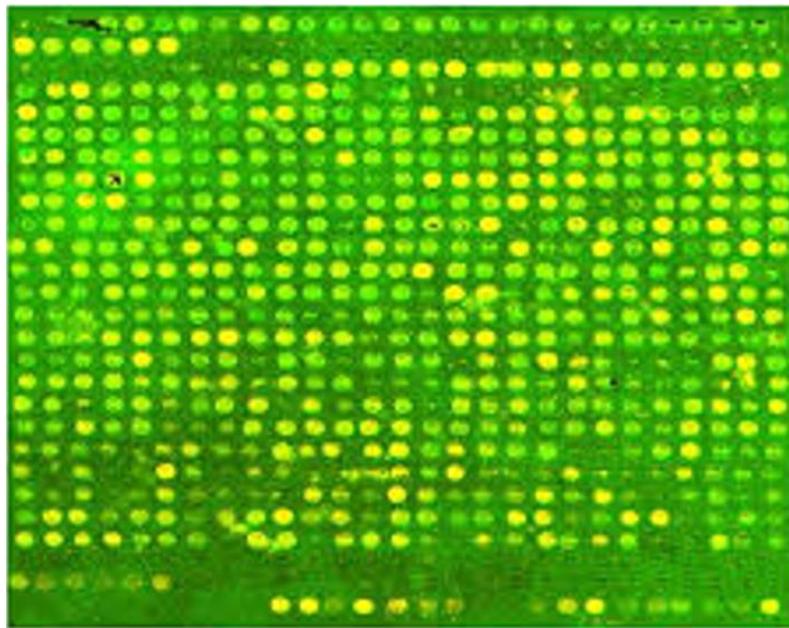
In summary, the statistical wavelet coefficient modelling method makes use of the wavelet coefficients' statistical characteristics to improve the modelling of visual data. The editing of images and videos is one instance where this strategy can be especially helpful.

### 2.2.3. Data-Adaptive Transforms

In recent reviews, a breakthrough technology named Independent Component Analysis (ICA) got drawn much interest. Authors in [Kaur and Singh \[31\]](#) proposed a reassessment of the ICA approach. One of the advantages of employing ICA is that it assumes a non-Gaussian signal, which makes it easier to denoise images with both non-Gaussian and Gaussian distributions. The computational cost of ICA-based approaches is higher than wavelet-based methods since it adapts sliding window and need an illustration of noise-free information or minimum of 2-frames from the same region. It may be challenging to obtain training data that does not have noise in some applications.

### 2.2.4. Advances in Microarray Image Enhancement

A review of the literature found that microarray image enhancement has received a significant amount of attention. [Mastriani and Giraldez \[20\]](#) proposed a new wavelet-based approach to give a denoising approach for removing noise sources and ensuring enhanced gene expression. Smoothing of co-efficients in the wavelet domain was used to achieve denoising. Based on Variational Mode Decomposition, [Kumar, et al. \[32\]](#) proposed a novel noise reduction approach capable of Variational Mode Decomposition(VMD). [Shao, et al. \[33\]](#) proposed a compressed sensing-based noise reduction approach. The correlation coefficient was employed to improve the efficiency of the search. [Shao, et al. \[33\]](#) uses quantitative analysis approach to evaluate the performance of proposed system, and achieved better Normalized Mean Squared Error (NMSE), MSE, Peak Signal-to-Noise Ratio (PSNR), and Root Mean Square (RMS) values to denoise cDNA microarray images. A sub grid of a microarray picture is shown in [Figure 2](#).



**Figure 2.** Sub grid of microarray image (Database: TBDB, ID: 422471).

## 3. CONCLUSION

This study provides an overview of some of the existing spatial and frequency domain approaches. Researchers have made numerous assumptions about elements such as the type of thresholding utilized, parametric assumptions, and decomposition levels in most of the methods offered. Some researchers assumed that the only noise models available were impulse, Gaussian, and fluorescence noise. This assumption may cause foreground pixels to be

misclassified as background pixels during the segmentation process, affecting gene expression levels. The MSE, structural similarity index measure (SSIM), contrast-to-noise ratio (CNR), and Noise Quality Measure (NQM) are some of the performance metrics that are utilized to measure the quality of denoised images in existing works. It is necessary to develop a denoising approach that can increase image quality by refining the image in terms of noise.

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