

A Study on Denoising Techniques for Microarray Images

Priya Nandihal¹ and Dr. Manjunath .S.S²

¹Assistant Professor, Dayananda Sagar Academy of Technology and Management
Email: talk2priya.nandihal@gmail.com

²Professor and Head, Dayananda Sagar Academy of Technology and Management
Email: mnj_ss2002@yahoo.co.in

Abstract— Microarray technology has transformed the field of genomic research by allowing the simultaneous profiling of thousands of genes. The microarray process is based entirely on the accurate extraction of quantitative information from images. Several types of noises are caused by the imperfection in generation of microarray images which affects accurate gene expression profiling. Spot recognition is difficult task as noise sources during image acquisition damages the image. Thus, Denoising is one of the major pre-processing steps in microarray image analysis. This paper presents an overview of some of the popular methods used to denoise microarray images both in spatial and frequency domain. The performance metrics used to measure the image quality after denoising is also discussed.

Index Terms— Microarray experiment, spatial filters, transform domain filters, performance metrics.

I. INTRODUCTION

Microarray technology was invented in 1995 and since that, it has been used as an important technology for gene study. Microarray is a chip that contains abundant Deoxyribonucleic Acid (DNA) sequence with its own unique location for each spot, allowing estimation of expression levels of thousands of genes simultaneously [1]. The importance of microarray is to unveil hidden biology of biological processes, monitoring gene expression levels, and for drug and treatment development; for example, therapeutic drugs for gene expression levels of cancer. By analyzing and comparing normal versus abnormal microarray gene expression profiling, genes involved in that particular disease can be identified. Due to its importance in pharmaceutical and clinical research, many applications for microarray have been developed to analyze them. Microarray can be processed through three steps [2]: (i) gridding, which is a process of assigning the location of each spot, (ii) segmentation, which is a process of grouping the pixels with similar features and finally (iii) information extraction, which calculates red and green foreground intensity pairs and background intensities. These experiments, like any other, are prone to noise. Measurement of gene expression levels can be influenced by the noise introduced to the data during the preparation, hybridization and scanning phase. Additive or multiplicative Gaussian, Poisson and exponential noise models have been used to describe the noise which affects microarray images [3][4][5]

Several methods have been proposed for eliminating and reducing the noise [6], [7] in microarray images. Two popular domains are the spatial filtering and the frequency domain approach. In the spatial filtering

methods, linear and nonlinear filters are used to reduce the noise. In the frequency domain case, the images are transformed using Fourier or Wavelet transformations and processed for noise reduction and finally inverse transformed to get back the denoised images.

The rest of the paper is organized as follows: Section 2 provides an overview on microarray experiment; Section 3 provides the survey on different denoising techniques in spatial domain; Section 4 describes different denoising methods in transform domain approach and section 5 discusses the performance metrics to measure the quality of image after denoising.

II. MICROARRAY IMAGE DENOISING IN SPATIAL DOMAIN

In this section, some of the popular methods for denoising a DNA microarray image in spatial domain from the literature are discussed.

Guifang Shao et.al, [14] has proposed a method for quantitative evaluation based on grid line number. The noise removal method proposed here consists of two parts: reducing edge noise and reduction of highly fluorescence noise. On the horizontal and vertical projections, the edge detection was applied on the microarray images. As linear replacement is fast mean and also easy, it is used in removing the fluorescent noise. It is compared with other methods of common noise reduction.

Weng Guirong and Su Jian [15] have proposed expectation maximization based microarray image segmentation for spot segmentation, which is to differentiate them from the background pixels. Along with expectation maximization, mathematical morphological filtering and morphological process is also presented. Mathematical morphology helps in eliminating the additive noise in images.

Islam Abdul-Azeem Fouad and Mai Said Mabrouk [16] has introduced a preprocessing step. The method includes a global background noise correction which removes gray values present in background by comparing with median value, contrast enhancement which improves the contrast between foreground and background; remove flare noise by applying morphological operations.

Rastislav Lukac et.al, [17] has proposed data adaptive approach to eliminate noise. The method tunes noise attenuating and detail preserving characters of filter through adaptively determined weighting coefficients by using spectral and spatial correlation of cDNA image. The member function uses an aggregated absolute difference which is performed for noise removal.

M. Emre Celebi et.al, [18] has proposed fast switching filter to eliminate impulsive noise from color images. The filter uses HSL color space, and it is based on the concept of peer group allowing detecting the noise fast in neighborhood without resorting pairwise distance computed in between pixels. If the neighborhood has pixels similar to it, then neighbourhood's center pixel is considered to be noise-free. Otherwise, result of vector median filter replaces it.

Mukhopadhyay [19] uses multi scale morphology method to enhance gray level image. The method focuses on nonlinear image enhancement as fundamental concept is to extend the general contrast enhancement technique. The method extracts shape and size features of image. Multiscale top-hat transform and bottom hat transform helps in extracting intensity of certain features in image. Multiple morphological towers are built to erect the image features so far formed. Combination of iterative weights of image which are put in different towers will enhance the image locally.

T. Chen [20] uses mathematical morphology edge detection which is dependent on pseudo top-hat transform derivative of top-hat transform. This preserves the details of edges prominently. Generally, the gradient property and threshold technique are used for edge detection. Using these methods the fine details of edges are eliminated that were presented in the darker region of image. Pseudo top-hat transformation is used to differentiate small grey level variations present in darker region. Gray level edge image is threshold to binary edge image through recursive quad-tree decomposition. The smooth edge features of darker region helps PTHT detect the edges well compared to other edge detection methods.

Ritika [21] discusses about contrast enhancing of medical images by morphological operations. Multi-scale structuring element is used in the work. At various scales of structuring element, dark and bright features of image are extracted at different scale. These extracted features and the original image are merged to reconstruct enhanced image. The method gives satisfactory visual result and but it could still reduced noise amplification.

Sandeep et.al, [22] dealt with images having problems of low contrast. Image enhancement includes the operations of contrast enhancement, quality of image improvement. The authors also present mathematical morphological analysis along comparing with different methods to address low contrast image. Usually

histogram equalization method is commonly used for contrast enhancement of digital images. Another method used is Contrast Limited Adaptive Histogram Equalization (CLAHE). This improves the contrast without noise amplification. White and black top hat transforms are the methods used in morphological contrast enhancement. These transform are applied at single scale or can be applied at multiple scales of structuring element which can be different size and shape.

Ram Murugesan and V.Thavavel [23] has proposed two-phase scheme for restoring the microarray images in the first phase, the pixels affected by the noise are determined by the adaptive median filter, while in second phase, special regularization method is applied on noisy pixels determined in the first phase to restore the image.

III. MICROARRAY IMAGE DENOISING IN FREQUENCY DOMAIN

The survey of different methods used for microarray image de-noising in frequency domain is discussed in this section.

Li Ying and Cui Li [24] have constructed adaptive tensor wavelets to denoise microarray image. The adaptive tensor model is combined with hidden markov tree model and novel method for denoising the microarray images. This shows extensive improvement in denoising. The hidden Markov tree (HMT) model is used to capture the key features and the complex features of real world data. It is observed that HMT also captures the secondary properties of wavelet transforms. A framework for adaptive wavelet is presented in this work which is used for denoising image. Adaptive tensor wavelet is assembled in order to denoise microarray image expressed in specific parameterizations of the univariate orthogonal scaling services.

Chaitra Gopalappa and T. K. Das [25] has discussed a method of identification and elimination of hybridization and scanning for noise present in microarray images, by making use of multiresolution analysis of dual-tree complex wavelet-transform-based which is combined with bivariate shrinkage thresholding.

Tamanna H and Yogendra P [26] has developed two bivariate estimators for microarray image denoising based on CWT by utilizing standard maximum a posterior and criteria of estimating linear minimum mean squared error. The method discussed here is capable of denoising by considering both interchannel signal and the noise correlations. The strength of the work is that the bivariate estimators includes the information about image correlation and also noise present between green and red channels of the image.

Ali Zifan et.al, [27] has presented a denoising approach in order to deal with noise inherent in microarray image. The decimated and the undecimated multiwavelet denoising capabilities are used to eliminate the noise present in the microarray data. Multiwavelet transforms gives sparser representation of signals than wavelet transforms with proper initialization in order that their difference from noise may also be clearly recognized. The denoising approach discussed here is capable of eliminating noise and guarantees that the gene expression would be better. This is possible because multiwavelet has ability to decompose a signal into time and frequency space. This also helps in study of non-stationary signals whose parameters increases overtime like noise and transients.

Hara Stefanou et.al, [28] introduces a two-stage approach for eliminating the noise which processes the multiplicative and additive component of noise. The signal is decomposed through multi-resolution transform and then considers sub-band decomposition multi-scale correlation and its weighted tailed statistics.

Darshana M [29] has proposed a method to deblur image using wiener filter along with point spread function (PSF) information of damaged blurred image by additive noise. Wiener deconvolution restores the image as it works in frequency domain which attempts in minimizing the effect of noise deconvolution at low poor signal to noise ratio frequency. Full auto correlations function is utilized in restoration of noisy and blurred images, which is recovered by fast Fourier transfer shifting.

Mantosh [30] has introduced a new method called Visushrink to denoise microarray images. But it does not give image of good quality due to elimination of large number of coefficients by the technique called soft threshold. To improve visual quality of image, soft thresholding method modifies the coefficients. This method is applicable for all levels of noise values.

Ravi Mohan Rai and Urooz Jabeen [31] have proposed wavelet based bivariate shrinkage method to denoise medical images. Noise speckle image is scaled and translated into representation of multiresolution analysis by implementing wavelet transform. At various levels of resolution, the noise speckle is reduced using bivariate shrinkage function. This operation is altered to give better results. Line and edge in the image are preserved much than results obtained from other standard filter methods. The time consumed by the modified

bivariate and bivariate method is less than other methods. Modified bivariate function results better in both SSIM and PSNR quality metrics.

IV. PERFORMANCE METRICS

The following performance metric are discussed to measure the quality of denoised image,

A. Mean Square Error(MSE)

Let $f(i,j)$ be the original image, $f'(i,j)$ be approximation of $f(i,j)$ that results from denoising original image. For any value of i and j , the error $e(i,j)$ between $f(i,j)$ and $f'(i,j)$ is given by $e(i,j)=f(i,j)-f'(i,j)$. So the total error between two images $e(x, y)=\sum\sum f(i,j)-f'(i,j)$, where the images are of size $M \times N$. The mean square error (MSE), between $f(i, j)$ and $f'(i,j)$ is then the squared error averaged over the $M \times N$ array given by,

$$MSE = \frac{1}{M \times N} * \sum_{i=1}^M \sum_{j=1}^N (f(i,j) - f'(i,j))^2 \quad (1)$$

B. Structural Similarity Indices (SSIM)

The **structural similarity index measures** the similarity between two images. It is very nearly consistent with human eye perception. Thus SSIM measure is accepted as a better method of measuring the similarity between two images than MSE. The SSIM between images x and y is given by ,

$$SSIM(x, y) = \frac{(2\mu_x \mu_y + C_1)(2\sigma_{xy} + C_2)}{(\mu_x^2 + \mu_y^2 + C_1)(\sigma_x^2 + \sigma_y^2 + C_2)} \quad (2)$$

μ_x the average of x ;

μ_y the average of y ;

σ_x^2 the variance of x ;

σ_y^2 the variance of y ;

σ_{xy} the covariance of x and y ;

$c_1=(k_1L)^2$, $c_2=(k_2L)^2$ are two variables to stabilize the division with weak denominator;

L the dynamic range of the pixel-values

$K_1=0.01$ and $k_2=0.03$ by default.

An SSIM value of 1 indicates perfect matching between x and y .

C. Contrast to Noise Ratio (CNR)

Contrast to Noise Ratio (CNR) is one of the measures utilized in specifying the quality of image. It is defined as,

$$CNR = \frac{\mu_0 - \mu_B}{\sigma_B} = \frac{\Delta \mu}{\sigma_B} \quad (3)$$

Where coefficient of defined structure's mean attenuation is represented by μ_0 and mean attenuation coefficient of background in the image surrounded by the defined structure is represented by μ_B . The σ_B is background noise expressed in terms of standard deviation of pixels that lies outside the region of interest area.

D. Noise Quality Metric (NQM)

The enhanced image and original images are simulated and are denoted by $O_s(x, y)$ and $I_s(x, y)$ respectively, the Noise Quality Metric (NQM) is given ,

$$NQM = 10 \log_{10} \left(\frac{\sum_x \sum_y O_s^2(x, y)}{\sum_x \sum_y (O_s(x, y) - I_s(x, y))^2} \right) \quad (4)$$

V. CONCLUSION

This paper presents an overview of some of the existing methods both from spatial and frequency domains. Most of the methods proposed by researchers have made various assumptions on factors such as type of

thresholding used, parametric assumptions and decomposition levels. Some of the researchers have assumed noise models to be only impulse, Gaussian and fluorescent noise. This assumption may lead to misclassification of foreground pixels to background pixels in the segmentation process and finally affects gene expression levels. This paper also discusses some of the performance metrics which are used to measure the quality of denoised image such as MSE, SSIM, CNR and NQM. A denoising method is to be designed which can improve the image quality by refining the image with respect to structural content, edges, textures and presence of noise. It can be further used for accurate measurement of gene expression profiling.

REFERENCES

- [1] John Quackenbush (2001), Computational analysis of microarray data, *Nat. Rev. Genet.*, pp.418-427.
- [2] N. Giannakeas and D. I. Fotiadis(2009), An automated method for gridding and clustering-based segmentation of cDNA microarray in *Computerized Medical Imaging and Graphics*, vol. 33,pp. 40-49.
- [3] R. Lukac, K. N. Plataniotis, B. Smolka, and A. N.Venetsanopoulos(2004),A multichannel order-statistic technique for cDNA microarray image processing,*IEEE Trans. Nanobiosci.*, vol. 3, no. 4, pp. 272–285.
- [4] Y. Balagurunathan, E. R. Dougherty, Y. Chen, M. L.Bittner, and J. M. Trent(2002), Simulation of cDNA microarrays via a parameterized random signal model, *J. Biomed. Opt.*, vol. 7, no. 3, pp. 507–523.
- [5] S. W. Davies and D. A. Seale (2005), DNA microarray stochastic model, *IEEE Trans. Nanobiosci.*, vol. 4, no. 3, pp. 248–254.
- [6] Mastrogianni Aikaterini, DermatasEvangelos and BezerianosAnastasios, Robust pre-processing and noise reduction in microarray images", *Proceedings of the fifth International Conference: biomedical engineering*,pp.360-364.
- [7] B. Smolka, R. Lukac, K.N. Plataniotis (2006),Fast noise reduction in cDNA microarray images", *23rd Biennial Symposium on Communications*, pp.348-351.
- [8] Zuva, T, Olugbara, S O Ojo, and S M Ngwira (2011), *Image Segmentation, Available Techniques, Development, and Open Issues 2*,vol. 3: pp. 20-29.
- [9] Abdul Khalid, N. E., N. Samsudin, and R. Hashim (2012), Abnormal Gastric Cell Segmentation Based on Shape Using Morphological Operations. *ICCSA. Salvador De Bahia: LNCS*, pp. 728-738.
- [10] <http://www.genome.gov>.
- [11] Lee, M L, F C Kuo, G A Whitmore, and J Sklar(2000), Importance of Replication in Microarray Gene Expression Studies: Statistical Methods and Evidence from Repetitive cDNA Hybridization." *Proc Natl Acad Sci U S A*, pp. 9834-9839.
- [12] Yang, Y H, M J Buckley, S Dudoit, and T P Speed(2000). Comparison of Methods for Image Analysis of cDNA Microarray Data..
- [13] Brown, P. O., Botstein (1999), Exploring the New World of the Genome with DNA Microarrays *Nature America Inc.*, pp. 33-37.
- [14] Guifang Shao, Hong Mi, Qifeng Zhou and Linkai Luo (2009), Noise Estimation and Reduction in Microarray Images, *World Congress on Computer Science and Information Engineering*.
- [15] Weng Guirong and Su Jian (2009), Microarray Image Processing Using Expectation Maximization algorithm and Mathematical Morphology, *International Joint Conference on Computational Sciences and Optimization*.
- [16] Islam Abdul-Azeem Fouad and Mai Said Mabrouk (2012), Developing a New Methodology for De-noising and Gridding cDNA Microarray Images, *Cairo International Biomedical Engineering Conference*.
- [17] Rastislav Lukac, Konstantinos N. Plataniotis, Bogdan Smolka, and Anastasios N. Venetsanopoulos (2005), A Data-Adaptive Approach to cDNA Microarray Image Enhancement, pp. 886–893.
- [18] M. Emre Celebi, Hassan A. Kingravi, Bakhtiyar Uddin and Y. Alp Aslandogan (2007), A Fast Switching Filter for Impulsive Noise Removal from Color Images, *Journal of Imaging Science and Technology*, Vol.51(2), pp: 155–165.
- [19] S. Mukhopadhyay and B. Chanda (2004), Local Contrast Enhancement of Grayscale Images using Multi-scale Morphology.
- [20] T. Chen, Q.H. Wu, R. Rahmani-Torkaman and J. Hughes (2001), A Pseudo Top-Hat Mathematical Morphological Approach To Edge Detection In Dark Regions, *Pattern Recognition Society. Published by Elsevier Science*.
- [21] Ritika (2012), A Novel Approach for Local Contrast Enhancement of Medical Images using Mathematical Morphology, *IRACST - International Journal of Computer Science and Information Technology & Security (IJCSITS)*, Vol. 2(2).
- [22] Ritika and Sandeep Kaur (2013), Contrast Enhancement Techniques for Images- A Visual Analysis, *International Journal of Computer Applications*, Vol. 64(17).
- [23] Ram Murugesan and V.Thavavel (2007), A Two-phase Scheme for Microarray Image Restoration, *Vol. 2(4)*, pp: 317-320.

- [24] Li Ying and Cui Li (2008), Based Adaptive Wavelet Hidden Markov Tree for Microarray Image Enhancements, IEEE International Conference on Bioinformatics and Biomedical Engineering.
- [25] Chaitra Gopalappa, Tapas K. Das, Steven Enkemann, and Steven Eschrich (2009), Removal of Hybridization and Scanning Noise From Microarrays, IEEE Transactions on Nanobioscience, Vol. 8(3).
- [26] Tamanna Howlader and Yogendra P. Chaubey (2010), Noise Reduction of cDNA Microarray Images Using Complex Wavelets IEEE Transactions on Image Processing, Vol. 19(8).
- [27] Ali Zifan, Mohammad Hassan Moradi and Shahriar Gharibzadeh (2010), Microarray Image Enhancement By Denoising Using Decimated And Undecimated Multiwavelet Transforms, Signal Image and Video processing, Vol. 4(2), pp: 177- 185.
- [28] Mario Mastriani, and Alberto E. Giraldez (2007), Microarrays Denoising via Smoothing of Coefficients in Wavelet Domain, International Journal of Electrical, Computer, Energetic, Electronic and Communication Engineering Vol. 1(2).
- [29] Darshana Mistry and Asim Banerjee (2014), Deblurred of Image with Wiener Filter in MATLAB, Journal of Emerging Technologies and Innovative Research (JETIR), Vol. 1(1).
- [30] Hari Om and Mantosh Biswas, A New Image Denoising Scheme Using Soft-Thresholding, Journal of Signal and Information Processing, pp 360-363, Volume 3, 2012.
- [31] Ravi Mohan Rai and Urooz Jabeen (2013), Analysis Techniques for Eliminating Noise in Medical Images Using Bivariate Shrinkage, Vol. 2(10).