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A Two-phase Scheme for Microarray Image Restoration

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Abstract. Microarray imaging is considered as an important tool for large scale analysis of gene expression. The accuracy of the gene expression depends on the experiment and image post processing. It's well known that the noises introduced during the experiment will greatly affect the accuracy of the gene expression. In this context, elimination of noise constitutes a challenging problem in microarray analysis. This paper proposes a two-phase scheme for removing impulse noise from microarray images by preserving the feature of interest. In the first phase, an adaptive median filter is used to identify pixels which are likely to be contaminated by noise. In the second phase, the image is restored using a specialized regularization method that is applied only to the noisy pixels identified during the first phase. The proposed scheme is developed as a reusable software component using the object oriented and platform independent features of JAVA. Finally, the performance of the proposed method was evaluated with microarray images collected from open source biological database. The results have shown a significant improvement compared to the conventional linear and nonlinear filters in terms of edge preservation and noise suppression.

Keywords: Image restoration, Denoising, Adaptive Median filters, Microarray Images.

1. Introduction

Microarray imaging is a recent cutting-edge technology in bioinformatics to monitor thousand of genes simultaneously. The origin of this imaging technique evolved from E. Southern's technique in the 1970s. It provided a systematic and comprehensive way to survey the DNA and RNA variations, which could become a standard tool for both molecular biology research and genomic clinical diagnosis, such as cancer diagnosis, type 1 and type 2 diabetes diagnoses [1].

In general, the results of the microarray processing combine two sample images which after image processing produce gene expression data for further analysis, such as gene clustering or identification. These three crucial steps, experiment, image processing and data analysis, determine the success of the microarray analysis [8]. Image processing plays a potentially large impact on the subsequent analysis. In recent years, large numbers of commercial tools have been developed in microarray image processing. The tasks of all these tools mainly focus on two major targets, namely: spot segmentation and spot intensity extraction [7]. However, the quality of the images from the experiments is not always perfect. The gene array experiments involve a large number of error-prone steps which lead to a high level of noise in the resulting images. Hence, the accuracy of the gene expressions derived from these images would largely affect the analysis process.

In this paper, we propose the application of a powerful two-phase scheme proposed in [2] for Microarray image restoration. The proposed scheme combines the variation method in [3] with the adaptive median filter [4]. More precisely, the noisy pixels are first identified by the adaptive median filter, and then these noisy pixels are selectively restored using an objective function with an l1 data fidelity term and an edge preserving regularization term. Since the edges are preserved for the noisy pixels, and no changes are made to other pixels, the performance of our combined approach is much better than that of either one of the methods.

2. Methodology

The noise originates from different sources during the course of experiment, such as photon noise,

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electronic noise, laser light reflection, dust on the slide, and so on. Hence, it is crucial to remove noise from the resultant image during this process. Exciting methods to reduce the noise source include using clean glass slide and using a higher laser power rather than higher PMT voltages. However, these are not adequate for the required image qualities. Hence this paper focuses on the implementation of the two-phase method to denoise microarray images.

2.1. Two-phase scheme

2.1.1. Adaptive median filter

To avoid the damage of good pixels in the microarray image, we propose a novel adaptive median filter that employs the switching scheme based on local statistics characters, which realizes the impulse detection by using the difference between the standard deviation of the pixels within the filter window and the current pixel of concern. The output of median filter applied to a pixel *Xij* is described as

$$Yij = median(\{Xi\text{-}s, j\text{-}t \mid (s, t) \in W\}) \tag{1}$$

Where *W* is a window of size w defined in terms of the image coordinates symmetrically surrounding the current or original pixel (i, j) as follows,

$$W = \{(k,l) : |k-i| \leq w \text{ and } |j-l| \leq w \} \tag{2}$$

Adaptive median filter employed in this paper, perform the following steps for each pixel location (i, j).

Initialize w = 3

1. Compute $s_{ij}^{min,w}$, $s_{ij}^{max,w}$ and $s_{ij}^{med,w}$, which are the minimum, maximum and median of the pixel values in S_{ij}^{w} respectively.
2. if $s_{ij}^{min,w} < s_{ij}^{med,w} < s_{ij}^{max,w}$, then go to step 5. otherwise increment w by 2
3. if $w \leq w_{max}$, go to step 2. otherwise replace Yij by $s_{ij}^{med,wmax}$
4. if $s_{ij}^{min,w} < y_{ij} < s_{ij}^{min,w}$ then y_{ij} is not a noise candidate, else replace y_{ij} by $s_{ij}^{med,w}$

The adaptive structure of the filter ensures that most of the impulse noises are detected even at a high noise level provided that the window size is large enough. Notice that the noise candidates are replaced by the median $s_{ij}^{med,w}$, while the remaining pixels are left unaltered. However, the replacement methods in this denoising scheme cannot preserve the features of the images; in particular the edges are smeared.

2.1.2. Edge preserving Regularization

After applying the adaptive median filter to the noisy image X in the first phase, the noisy pixels in filtered image Y takes values in the set $\{s_{min}, s_{max}\}$, we define the noise candidate set as,

$$N=\{ (i,j) \in A : Y_{ij} \neq X_{ij} \text{ and } X_{ij} \{s_{min}, s_{max}\}\}, \tag{3}$$

where A is the size of the image. The set of all uncorrupted pixels is $N^c = A \setminus N$. Considering a noise candidate, at (i,j) ∈ N. Each of its neighbors (m,n) ∈ V_{ij} is either a correct pixel or corrupted pixel. The neighborhood V_{ij} of (i,j) is thus split as $V_{ij} = (V_{ij} \cap N^c) \cup (V_{ij} \cap N^c)$. Noise candidates are restored by minimizing the objective function restricted to the noise candidates set N,

$$F_y |_N (u) = \sum_{(i,j)\in N} [| u_{ij} - y_{ij} | + \frac{\beta}{2}(S_1 + S_2)] \tag{4}$$

where

$$S_1 = \sum_{(m,n)\in V_{ij} \cap N^c} 2\delta(u_{ij} - y_{mn})$$

$$S_2 = \sum_{(m,n)\in V_{ij} \cap N} \delta(u_{ij} - u_{mn})$$

$$\delta(t) = \sqrt{\alpha + t^2}, \quad \alpha > 0$$

$$\delta(t) = | t |, \quad 1 < \alpha \leq 2$$

With choice of β, the minimizer u of Fy satisfies $u_{ij}=y_{ij}$ for most of the uncorrupted pixels y_{ij}. Furthermore, all pixels u_{ij} such that $u_{ij} \neq y_{ij}$ are restored so that edges and local features are well preserved, provided that is an edge preserving potential function.

3. Design and Implementation

The object-oriented approach used to develop the restoration system encourages code reusability and guarantees more consistent behavior within the application by giving a strong focus on class structure. JAVA is the most productive tool to implement object-oriented approach for the development of windows-based software, without sacrificing flexibility and performance [5]. Hence, JAVA was selected for designing class hierarchies for the present system. The cost of future enhancements will also be reduced because of the polymorphism and inheritance features that enable the extension of the application to other medical images.

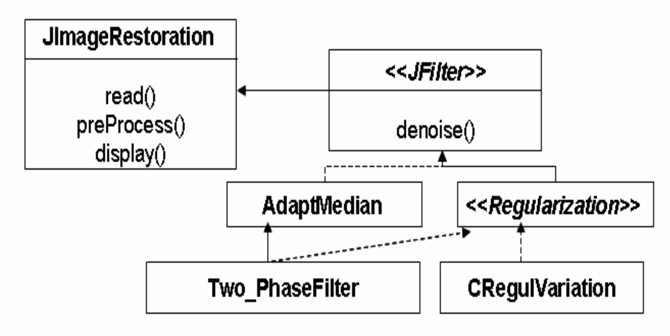


Fig. 1: Class hierarchy of Microarray Image Restoration system

User-defined subclasses were created from JFC super classes. The methods for constructors, destructors, exception handling, loading images and denoising were developed as member functions of the subclasses. The object of *JImageRestoration* binds all objects of three subclasses and runs their methods. *Init( )* method of initializes the overall restoration system. The restoration procedures of the system are outlined in a class hierarchy diagram shown in the Fig 1. The pixel values of the image are grabbed as gray scale value using the *read()* method. The grabbed pixels are filtered using the services provided by the *JFilter* interface. The interface *JFilter* is implemented by the class *Adaptmedian* as well as it is inherited by the interface Regularization. The proposed two-phase scheme inherits the services of both *AdaptMedian* and *Regularization*.

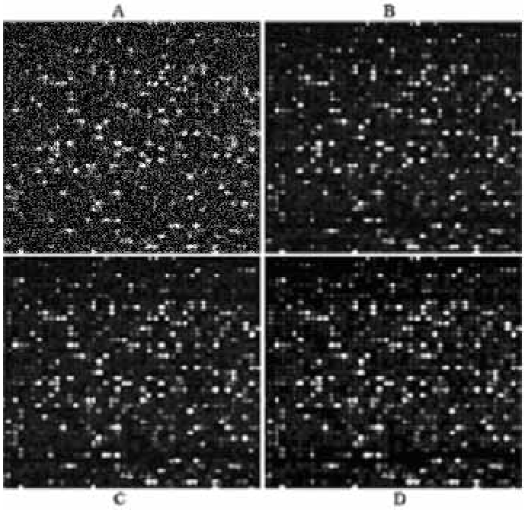
4. Results and Discussions

A comparative analysis of the proposed method with conventional adaptive Median and Wiener filter is presented to validate the results obtained. The Signal to Noise Ratio (SNR) used to evaluate the restoration performance quantifies how well one can resolve a true signal from the noise of the system. It is clear that when the SNR is low, the intrinsic variation in the data is high and confidence in the accuracy of the data is low. For a microarray image, the SNR of a target spot is defined as [6],

$$SNR = \frac{S_p - B_p}{\sigma_p}. \quad (5)$$

Sp is the mean intensity of the target spot; *Bp* is the mean intensity of the local background; *σp* is the standard deviation of the local background.

As an illustration, Fig. 2 shows the results for a microarray image corrupted with 50% of salt and pepper noise. One can observe that the proposed filter preserves edge sharpness and reduces many artifacts in contrast to the other well performing algorithms such as adaptive median and wiener filter. In addition, the plot for numerical results in SNR for the same image at various noise levels is given to its right. It can be inferred from the SNR plot that the proposed denoising scheme shows a significant SNR even when the noise level is high. This is mainly based on the accurate noise detection by the adaptive median filter and the edge preserving property of the variational method of [4].



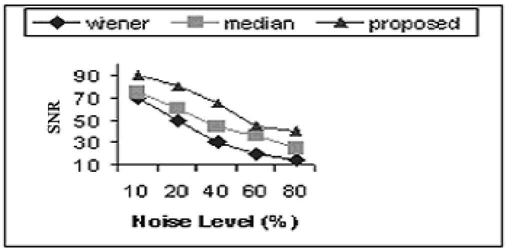


Fig 2: Visual comparison of restoration results of different filters: Wiener filter (B), Adaptive Median filter (C) and the proposed denoising scheme (D) on the corrupted microarray image with 50% impulse noise (A). SNR plot for Microarray image at various noise levels (To the right).

5. Conclusions

In this paper, we propose a decision-based, detail-preserving restoration method to deal with microarray image restoration. It is the ultimate filter for removing noise by preserving the feature of interest especially edges. The simulation results applied on microarray image show that our method performs much better than the conventional linear and non-linear filter. The application of this method would improve the accuracy of gene expression, and therefore easily identify the diseased gene for diagnosing critical diseases.

6. References

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