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Adaptive Data Clustering Algorithms For Microarray Image Analysis

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Abstract:
By adopting Microarray Technology, in a single study one may analyse the function of thousands of genes in parallel. Microarrays are utilised in different applications including illness diagnostics, medication development and bio-medical research. A Microarray picture has thousands of spots and each of the spot contains multiple copies of one DNA sequence. The analysis of microarray picture is done in three stages: gridding, segmentation and information extraction. The microarray image analysis takes the spot intensity data as input and provides the spot metrics as output which are utilised in categorization and identification of differentially expressed genes. The intensity of each area shows the expression level of the given gene. Generally, clustering methods are employed for the segmentation of microarray pictures. These algorithms have the benefits that they are not bound to a certain spot size and form, does not need an initial state of pixels and have no requirement for post-processing. These methods have been built based on the knowledge about the intensities of the pixels solely. Clustering algorithm such as K-means, Fuzzy c-means etc., has been utilised in the literature. The basic prerequisite for every clustering technique is the number of clusters K. Estimating the value of K is challenging assignment with given data. This work introduces adaptive data clustering algorithms which delivers appropriate segmentation results with easy operation and eliminates the interactive input K (number of clusters) value for segmentation of microarray picture. The qualitative and quantitative findings reveal that adaptive data clustering algorithms are more effective than standard data clustering algorithms in segmenting the spot region, thereby providing more accurate expression-ratio.

Keywords: Image processing, Microarray Image Analysis, Clustering methods

1. INTRODUCTION:

Several interpolation functions are employed in the decomposition of the picture in this paper to show a noise reduction approach using Bi-dimensional Empirical Mode Decomposition

(BEMD) and wavelets. Overall, the spot intensity data from the microarray image analysis is used to generate the spot metrics, which are then used to categorize and identify genes that are expressed differently on the microarray. The intensity of each area corresponds to the degree of gene expression for that specific gene. The segmentation of a microarray picture is often accomplished via the use of clustering techniques. The clustering algorithms K-means, Fuzzy c-means, and others have been used in the literature to classify data. For each clustering approach the degree of clusters K is a critical factor. Estimating the value of K from the available data is a challenging undertaking. This Paper describes adaptive data clustering methods that provide correct segmentation results with a single operation and do not need the user to enter a K (number of clusters) value during the segmentation of a microarray image segmentation process. Researchers have shown that adapting data clustering algorithms outperform standard data clustering algorithms in both formative and summative assessments when it comes to segmenting the spot region, resulting in more accurate expression-ratios than normal data clustering methods.

When evaluating microarray gene expression data, it is crucial to identify the genes that create comparable gene expression patterns. This is accomplished through the use of clustering techniques. Thus, the computational challenge of clustering and ranking gene expression data gets condensed into a single sentence inside this paragraph. Classifying data into groups is known as clustering that are similar to each other in terms of their properties and characteristics. In exchange for data simplification, it chooses to ignore certain details. Informally, clustering can be thought of as data modeling that summarizes the data in a concise manner. As a result, it has applications across a wide range of disciplines, from statistics to numerical analysis. When it comes to descriptive tasks, clustering is one of the most common. Based on their attribute values, it is used to identify homogenous groupings of things (dimensions). Cluster clustering methods have been widely researched in statistics, pattern classification, and machine learning. With K-means and Medoid approaches, the K cluster representatives are chosen and each item is allocated to a group with the closest representation, resulting in the total of squared distances between objects and their representatives being as little as feasible. Determining the density of an area and then grouping together things that are situated in the same dense area is what DBSCAN is all about. Clustering is a data analysis technique that uses a hierarchical series of divisions. It is possible to use an agglomerative hierarchical clustering to group objects together. This method begins by grouping each object into an atomic cluster, the items in the cluster are then joined into significantly larger clusters until they are all contained inside a single cluster. Divisive, hierarchical clustering is able to reverse the procedure by initiating with all of the items in the cluster and sub-grouping them into very smaller chunks at the beginning of the process.

2. LITERATURE

The Adaptive Circle (AC) segmentation algorithm might be considered as an improvement of the FC segmentation algorithm (Lehmussola et al., 2006). Similarly to the FC algorithm, It is assumed that all spots are circular using the AC algorithm. Each microarray spot's radius is determined independently in the AC technique and thus, the target mask, which provides the

spot’s foreground and spot’s background pixels, to adapt to various circular spot’s sizes (Li et al., 2005).

Understanding gene function, regulation, cellular processes, and cell subtypes has been aided by clustering algorithms [3]. It is possible to group together genes with comparable biological activities that have similar expression patterns (co-expressed genes). There are several genes whose roles have hitherto been unknown that might benefit from this method [13]. Because the genes in almost the same cluster are likely to be involved in the same biological processes, co-regulation may be seen in the expression levels of these genes. When genes in the same cluster have similar promoter DNA sequences, it is possible to identify regulatory patterns peculiar to each of the gene cluster and suggest cis-regulatory elements [15]. Gene expression data clustering also generates ideas about the transcriptional regulatory network's mechanism, which may be tested. As a last point, it is possible to find sub-cell types that cannot be identified using classic morphology-based techniques.

When using clustering techniques based on partitioning, data is divided into many divisions, each of which represents a cluster. In each division, each cluster's cluster centre is the location where all of the data points intersect. One of the most well-known examples of this kind of clustering technique is K-means clustering [29]. To be more exact, cluster centres are picked at random through using K-means clustering method, and each data point is allocated to a cluster centre based on its Euclidean distance from of the core of the cluster. Until the algorithm approaches convergence, it keeps resetting the cluster centres and then assigning every data point to a cluster [12]. However, since the cluster number is required as input, the K-means clustering technique cannot be used with a dataset that has an unknown cluster number. In addition, the setup of the cluster centres may give varied clustering outcomes on different runs of this technique [29]. Furthermore, K-means clustering algorithm measures the similarity by using the Euclidean distance which gives the same importance to all the data points without consider other factors such as density, dependent features, shape, patterns or scale of data points [30, 31]. For example, it is difficult for K-means clustering algorithm to separate non-convex clusters.

Yousef et al. analyzed the most commonly used machine learning algorithms for biomarker identification: clustering & support vector machines (SVM). They explored a variety of machine learning strategies, including supervised and unsupervised learning, as well as feature selection. According to their findings, combining several data mining approaches is the most effective way to uncover biomarkers. For more accurate biological outcomes, they recommend embedding biological knowledge into the algorithm.

In order to discover cancer biomarkers, Chen and colleagues used a network-constrained SVM technique [18] to merge gene expression as well as protein-protein interaction (PPI) data. Patients' clinical outcomes and biomarkers may be predicted and identified using PPI network information. Gene expression data and the PPI network are fed into classifiers in order to make predictions about the outcome of future experiments. A statistical significance summative assessment on the permutation of sample names found biomarkers. Breast cancer-related biomarkers were shown to have a high functional

relevance, and it was discovered that these biomarkers may be linked to the spreading of cancer cells.

Swan et al. [19] utilised proteomics data and machine learning to identify biomarkers. This work used a preprocessing technique known as "peak picking," which examines mass spectrometry data in search of peaks with unusually high signal intensities. Machine learning is used to find the best biomarkers from these peaks, which are regarded prospective biomarkers (proteins). However, this has the problem of necessitating more research. Additionally, additional preprocessing techniques, including as normalization, peak aligning, and noise - reducing approaches, are required to maximize accuracy and minimize errors.

Classification algorithms, statistics, and machine learning approaches all come together in the maximum difference subset algorithm proposed by Weiler et al. [20]. Class discovery, class prediction, and discovering dysregulated genes that trend differently from other genes in the same subtype are the three processes they defined for data analysis. The authors investigate the idea of using a clustering method in combination with a standard statistical analysis in order to locate the dysregulated genes. Five genes related to leukaemia were discovered using this method.

Biomarkers for subtype categorization were discovered by Miloli et al. [21] using a novel approach termed CM1 score. The CM1 score is a way of comparing the expression levels of two samples within the same class to one another. For breast cancer subtypes, they discovered 30 biomarkers using this method.

Alkhateeb et al. employed a time-series approach to linear interpolation transcript levels of expression throughout stages of cancer to uncover biomarkers for prostate cancer. Gene transcripts with a distinct trend than the others were filtered out using profile alignment and hierarchical clustering. Outlier identification may be improved by using a combination of a good clustering technique, a good distance function, and a good validity index.

3. NOISE REMOVAL USING BEMD PLUS WAVELETS

The amount of noise inside the microarray image would have effect on the performance of the edges that are retrieved from the image. Gridding of microarray pictures is conducted automatically using this edge information as a main source of data. A signal processing approach called empirical mode decomposition [5,6] separates any nonlinear and non-stationary signal into oscillatory functions without inflicting any harm to the original signal, utilising a shifting process. Two qualities must be met by each of these oscillatory functions, referred to as Intrinsic Mode Functions (IMF), before they can be called IMFs: (1) equal or a one-point increase or decrease in the total number of zero crossings and extreme points; and (2) each IMF must meet the above requirements. Symmetric envelopes with zero mean may be analyzed using local maxima and minima [7]. The original signal may be restored by combining IMFs and residue with the decomposed signal following non-destructive EMD decomposition, as shown by the results. One of the initial IMFs has a high frequency component; others range from the next high frequency down to the lowest. IMFs on a two-dimensional signal may be obtained using the shifting method as follows:

a) Consider the Microarray image I(x,y) that was utilised for EMD decomposition. In I, you may find all of the local maximum and minimum points (x,y).

b) Upper envelope is a slang term for Creating upper envelope Lw(x,y) is accomplished via interpolation of maxima points. Creating lower envelope Up(x,y) is accomplished through interpolation of minima points. This interpolation is accomplished out utilising the redial basis functions listed in Table 4.1 to get the desired result.

c) As shown by the symbol Mean, calculate the average of the bottom and upper envelopes (x,y).

$$Mean(x, y) = \frac{(Up(x, y) + Lw(x, y))}{2} \quad (1)$$

d) To calculate the average signal, remove the original signal and multiply the result by two.

$$Sub(x, y) = I(x, y) - Mean(x, y) \quad (2)$$

e) The existence of an IMF is determined by whether or not Sub(x,y) meets the IMF characteristics.

$$IMFi(x, y) = Sub(x, y) \quad (3)$$

f) When subtracting from an input signal, what you've taken out of the IMF. The value of I(x,y) has now been determined.

$$I(x, y) = I(x, y) - IMFi(x, y) \quad (4)$$

Steps (b) through (f) above should be repeated for the production of subsequent IMFs.

g) This technique is continued until I(x,y) does not include any maxima or minima points that may be used to form envelopes in the graph.

The original image may be recreated using the inverse EMD, which is defined as

$$I(x, y) = \sum IMFi(x, y) + res(x, y) \quad (5)$$

The BEMD-DWT algorithm might well be summarized as follows:

a)To get IMFi (i=1, 2,...k), use 2-D EMD with noisy microarrays. Residue is the name given to the kth IMF.

b) High frequency components are present in the first intrinsic mode function (IMF1), which makes it a good candidate for denoising. The mean filter is used to denoise this IMF1. Using the DNIMF1 symbol, we may express this de-noised IMF1.

c) It is possible to rebuild the denoised picture by summing DNIMF1 and the other IMFs as provided by

RI = DNIMF1□ □ IMFi (6)

R and RI are two distinct bands, with R being the reformed band. The BEMD-DWT filtering method is shown schematically in Figure 4.1.

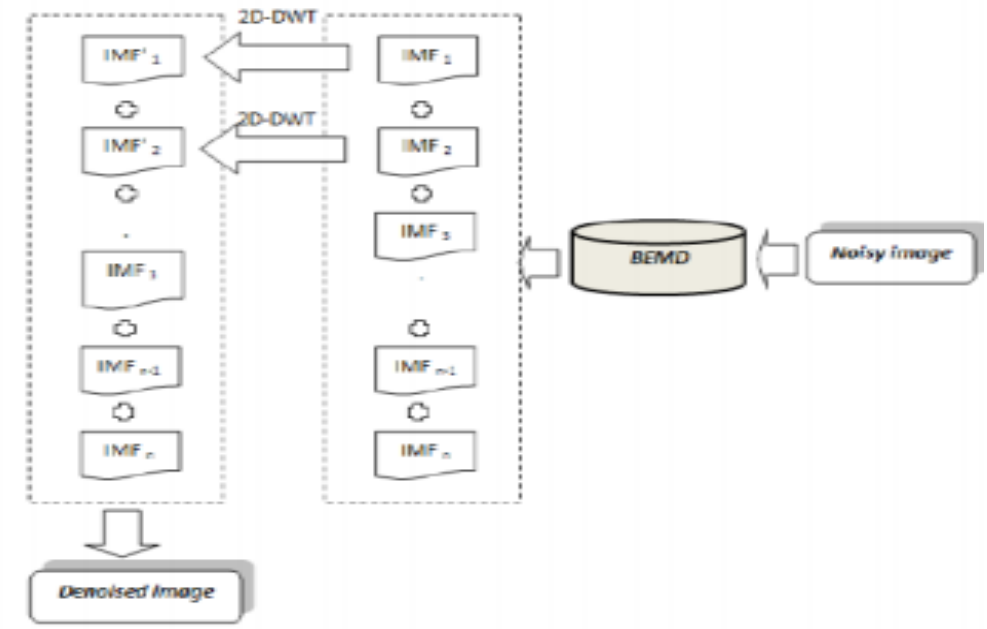


Figure 3.1: Image Denoising using BEMD + WAVELET

Function	Description
$\varphi(x) = x$	Linear function
$\varphi(x) = \sqrt{x^2 + 1}$	Multi Quadrique Function
$\varphi(x) = e^{-x}$	Exponential Function
$\varphi(x) = x\log(x)$	Logarithmic Function
$\varphi(x) = x^2\log(x)$	Spline Function

Table 3.1: Different Interpolation Functions

4 DATA CLUSTERING ALGORITHMS

4.1 K-means Algorithm

In this approach, each cluster is linked with a centroid, and the algorithm is based on centroid-based data. Data points and the clusters toward which they belong must be as close together as possible in order to achieve this goal.

Method of clustering using k-means is responsible for two primary tasks:

- It keeps trying to figure out the best value for K centre points or centroids through a process called optimization.
- K-centers are made up of points that are close to each other, and each point is given a k-center. It starts with the data points that are close to a certain "k-center" in the first place.

The following is a description of method of clustering using k-means [13] used for effective segmentation of microarray images:

1. Consider a random sample of K starting clusters {C1, C2,.....,Ck} drawn from the m*n picture pixels {I1, I2, I3,.....,Im*n}.
2. Then, for each pixel that matches the following requirement, it should be assigned to the cluster Cj(j=1,2,....K).

$$D(I_i, C_j) < D(I_i, C_q), q = 1, 2, ..., K$$
$$j \neq q \qquad (7)$$

In which D(.,.) is the measure of dissimilarity.

3. A new cluster centroid might well be found as follows:

$$C_i^{\wedge} = \frac{1}{n_i} \sum_{I_j \in C_i} I_j, i = 1, 2, ...K \qquad (8)$$

Where n_i seems to be the total number of pixels in the cluster C_i.

4. If $C_i^{\wedge} = C_i, i = 1, 2, ..K$ (9)

After that, you may quit.

Otherwise, go back to step 2.

4.2 K-medoids Algorithm

When using prototype-based techniques, the fundamental challenge is that they need the data points to be elements of a Euclidean space, which is necessary since we need to average the data points in some way. As a solution to this problem, K-medoids is an alternative form of K-means that makes use of objects from the data set as prototypes, i.e., instead of centroids, it makes use of medoids. Thus, it is no longer required to classify prototypes as a distinct group of objects (or an "average" object). Microarray images might well be segmented using the k-medoids clustering algorithm [14], which is described below:

1. A random sampling of the first K medoids is conducted $\{M_1, M_2, \ldots\ldots, M_k\}$ for the clusters $\{C_1, C_2, \ldots\ldots, C_k\}$ from the m*n pixels of image $\{I_1, I_2, I_3, \ldots\ldots, I_{m*n}\}$.

In the centre of a cluster, there is a cluster point known as a cluster medoid. In the cluster, it's the point that has the least sum of distances between it and all of the other cluster points.

2. The assignment of pixels to clusters is accomplished by the use of the condition provided by

$$D(I_i, M_j) < D(I_i, M_q), q = 1, 2, ..., K$$
$$j \neq q \qquad (10)$$

Where D(. , .) denotes the dissimilarity measure.

3. Identify and collect new medoids $M^{\wedge}_i$ that are part of a cluster. C_i , $i = 1, 2, ...K$. The pixel value that differs the least from all other locations is called this.

4. If

$$M_i^{\wedge} = M_i, i = 1, 2, ..K \qquad (11)$$

After that, you may quit.

Otherwise, go back to step 2.

4.3 Fuzzy c-means Algorithm

Data points are assigned a likelihood or probability score to indicate whether or not they are part of a cluster using the soft clustering approach known as Fuzzy C-Means. According to the following description, clustering method with fuzzy c-means [16] for segmentation of micro array images is used:

1. A random selection of K initial clusters $\{C_1, C_2, \ldots\ldots, C_k\}$ from the m*n pixels of image $\{I_1, I_2, I_3, \ldots\ldots, I_{m*n}\}$.
2. Here u_{ij} is initialised with values from 0 to 1 and m=2 in the membership matrix. It's essential that the total of the pixel memberships for each cluster be equal to 1.
3. Pixel assignment to clusters is done using the condition given by

$$u_{ij}^m D(I_i, C_j) < u_{iq}^m D(I_i, C_q), q = 1, 2, ..., K$$
$$j \neq q \qquad (12)$$

D(.,.) signifies the dissimilarity measure.

4. The following are the new membership as well as cluster centre values:

$$u_{ik} = \frac{1}{\sum_{j=1}^{K} \left(\frac{D(C_i, I_k)}{D(C_j, I_k)}\right)^{\frac{1}{m-1}}}, \; for 1 \leq i \leq K$$

The k^{th} object inside the i^{th} cluster is denoted by u_{ik}.

$$C_i^{\wedge} = \frac{\sum_{j=1}^{n} u_{ij}^{m} I_j}{\sum_{j=1}^{n} u_{ij}^{m}} \quad (13)$$

There are n pixels in the cluster C_i, and n is the number.

5. Repeat steps 2-3 until all objects have been allocated to the cluster with the maximum number of members [17].

4.4 ADAPTIVE DATA CLUSTERING

The underlying concept of any clustering method is to group the objects that are nearest to them by clustering the K points in the space in which they are located. The values of the cluster centers are modified one after the other in an iterative manner until the optimal clustering results are found. Making an accurate determination of the proper K value is critical to the success of any clustering technique. We have developed the adaptive clustering method with k-means in this Paper for the purpose of estimating the K-value; the same method may be used to the other algorithms discussed in this Paper.

Using the Euclidean distance, a similarity metric employed in the K-means algorithm, an initial cluster's centre vector is categorized. The error square sum model uses the error square sum criterion function as a clustering criteria function. It is difficult to estimate K since the K-means approach relies on a predetermined value, and the value of K must be determined in advance. A selection of K = 2 is used to begin the segmentation process, which results in two clusters being used to begin the segmentation process and a final cluster being used to finish the segmentation process. Finally, we may determine the total number of segmentation outcomes by using the maximum interconnected domain approach [20]. In this case, it is presumed that the K value was correctly determined based on the final segmentation result. To ensure that the series starts and ends with identical K values, the sequence's initial K value will be increased until it does. This approach for selecting a K-value may be used to clustering algorithms with K-medoids, K-modes, Fuzzy K-medoids and Fuzzy c-means which can be utilised to develop adaptive clustering algorithms.

In the next section, we will discuss the adaptive k-means clustering technique.

For K=2 to 10

{

Randomly consider K initial clusters $\{C_1, C_2, \ldots\ldots, C_k\}$ from the m*n pixels of image $\{I_1, I_2, I_3, \ldots\ldots, I_{m*n}\}$.

1. If the following condition is true, then each pixel should be assigned towards the cluster C_j {j=1,2,…..K}

$$D(I_i, C_j) < D(I_i, C_q), q = 1, 2, ..., K$$
$$j \neq q \quad (12)$$

The dissimilarity measure denoted by D(.,.)

2. Follow these steps to locate a new cluster centroid:

$$C_i^{\wedge} = \frac{1}{n_i} \sum_{I_j \in C_i} I_j, i = 1, 2, ...K \tag{13}$$

For each cluster C_i, n_i represents how often pixels belong to it.

3. If

$$C_i^{\wedge} = C_i, i = 1, 2, ..K \tag{14}$$

After that, you may quit.

Otherwise, go back to step 2.

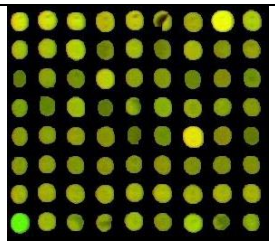
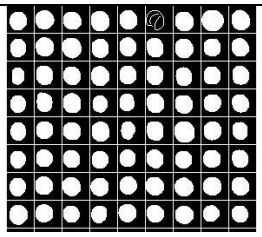
Compare the maximum connected domain results

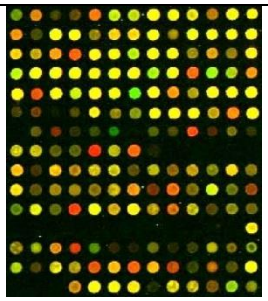
If equal to K print segmented result and break;

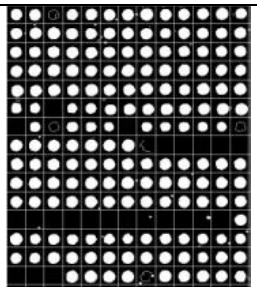
else continue with incremented value of K;

4.5 RESULTS AND DISCUSSIONS

When applied to two microarray pictures chosen from the stand alone microarray database that match to breast categorization a CGH tumour tissue, the suggested clustering technique yields the following results: M Image 1 has a total resolution of 38808 pixels, whereas MImage2 has a total resolution of 64880 pixels. The noise removal in microarray image is done using BEMD + Wavelets method. In BEMD decomposition process, the envelopes are created using different interpolation methods. Out of these spline interpolation gives better envelopes based on number of maxima and minima values. According to the approach provided in [18], gridding is done on the input pictures in order to divide the image into sub-compartments, with each sub-compartment containing just one and only spot area and one backdrop colour.

M Image 1	Gridded Image
	
M Image 2	Gridded Image



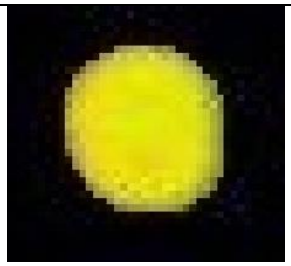


As shown in Figure 1, Compartment No. 1

Feature-based segmentation of a dataset fcm

image 2 of Compartment No 8

Segmentation with Adaptive K-means



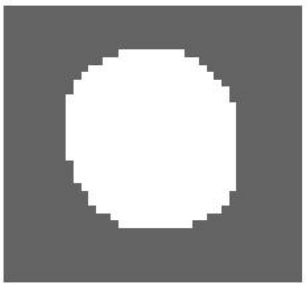


Figure 4.1 : Gridding and segmentation results

Table 4.1 shows PSNR values of different nonlinear filtering algorithms for different values of sigma (Gaussian Noise) added towards the image in-order to find the performance of the proposed noise removal algorithm [Done on M Image 1].

Table 4.1: PSNR values of Noise Removal

Noise level (Sigma)	Median	Wavelet	BEMD + Wavelet
5	34.2	35.7	**37.9**
10	29.5	32.5	**34.8**
15	25.4	27.3	**29.7**
20	21.1	23.2	**26.2**

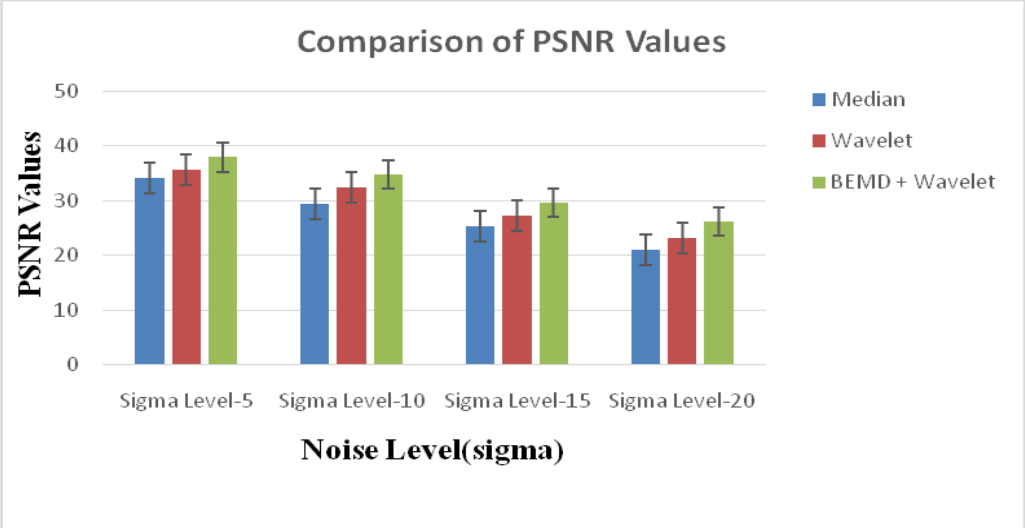


Figure 4.2: Comparatative Analysis of PSNR Values

Figure.4 specifies the outcome of the gridding algorithm. After dividing the picture into compartments in such a way that each and every compartment has a single spot and a single backdrop, it is found that the true image contains M Image 1's compartment 1 and M Image 2's compartment 8's compartment 1. The Adaptive K-means clustering algorithm is used to segment the image compartments and is detailed in full below. The outcomes of the segmentation method are shown in Figure 4.3.

Table 4.2: MSE values

	Normal Clustering		**Adaptive Clustering**	
Method	**Compartment No 1**	**Compartment No 8**	**Compartment No 1**	**Compartment No 8**
K-means	96.2	95.8	**95.9**	**94.5**
K-medians	95.1	94.2	**94.7**	**93.2**
K-mode	95.2	94.3	**94.8**	**93.6**
Fuzzy c-means	90.7	90.2	**90.01**	**89.6**
Fuzzy K-medoids	91.8	91.4	**90.2**	**90.1**

Table 4.2 displays the results of quantitative assessments of clustering methods performed using MSE [19, 20]. For segmenting the microarray picture, the findings demonstrate that the adaptive fuzzy c-means method delivers the lowest mean square error (MSE).

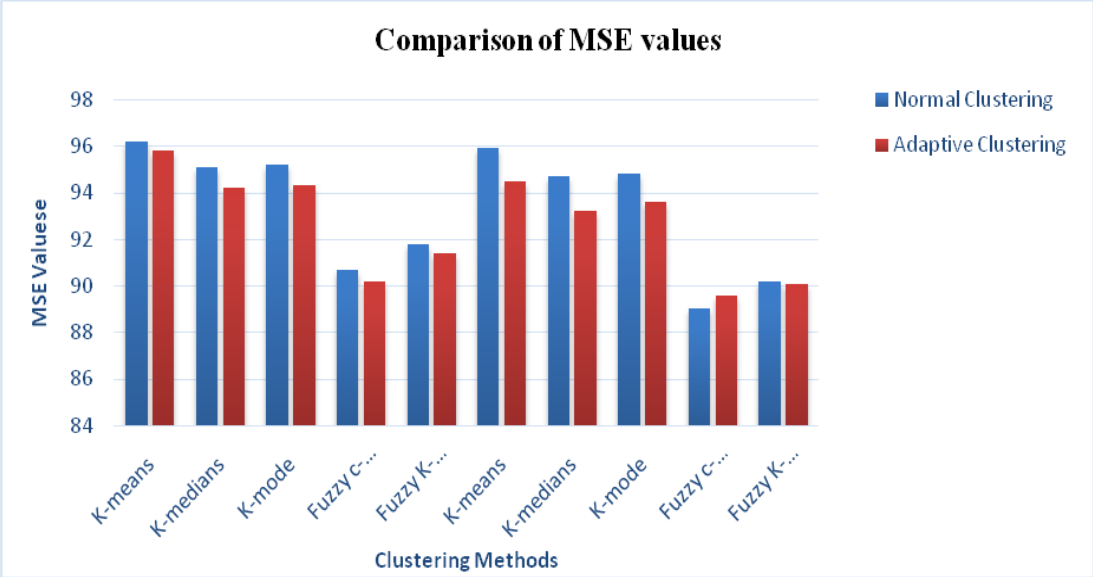


Figure 4.4: Comparitative Analysis of MSE Values

5. CONCLUSION

Using microarrays, hundreds of gene expression levels may be monitored in real time. Gridding, segmentation & information extraction are indeed the three main process states in microarray image analysis. This Paper represents a noise removal methodology using BEMD + Wavelets with different interpolation methods used in BEMD decomposition process. The segmentation of a microarray picture is accomplished via the use of adaptive clustering techniques. In this, k-means clustering will be the subject of our discussion. In way to construct these algorithms, the camera sensor's pixel intensities would have had to be known. The count of clusters K is one of the very important criteria for any clustering technique. Estimating the value of K from the available data is a challenging undertaking. This Paper describes adaptive data clustering methods that provide correct segmentation results with a single operation and do not need the user to enter a K (count of clusters) value during the segmentation of a microarray image segmentation process. Adaptive approach of data clustering outperform conventional data clustering algorithms in segmenting the spot region, as shown by qualitative and quantitative research, resulting in more precise expression ratios. The adaptive fuzzy c-means clustering technique, which is the most effective of the algorithms discussed in this Paper, delivers the best segmentation results. The log ratio of R/G is a measure of the gene's abundance of expression.

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