Study On Clustering Techniques And Application To Microarray Gene Expression Bioinformatics Data

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Dedicated to my parents

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Certificate

This is to certify that the work in the thesis entitled ” ***Study On Clustering Techniques And Application To Microarray Gene Expression Bioinformatics Data***” submitted by ***Kumar Dhiraj*** is a record of an original research work carried out by him under my supervision and guidance in partial fulfillment of the requirements for the award of the degree of *Master of Technology (Research)* in *Computer Science and Engineering* during the session 2007 – 2009 in the department of *Computer Science and Engineering, National Institute of Technology, Rourkela*. Neither this thesis nor any part of it has been submitted for any degree or academic award elsewhere.

Prof. Santanu Kumar Rath

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Kumar Dhiraj

Abstract

With the explosive growth of the amount of publicly available genomic data, a new field of computer science i.e., bioinformatics has been emerged, focusing on the use of computing systems for efficiently deriving, storing, and analyzing the character strings of genome to help to solve problems in molecular biology. The flood of data from biology, mainly in the form of DNA, RNA and Protein sequences, puts heavy demand on computers and computational scientists. At the same time, it demands a transformation of basic ethos of biological sciences. Hence, Data mining techniques can be used efficiently to explore hidden pattern underlying in biological data. Un-supervised classification, also known as Clustering; which is one of the branch of *Data Mining* can be applied to biological data and this can result in a better era of rapid medical development and drug discovery.

In the past decade, the advent of efficient genome sequencing tools have led to enormous progress in life sciences. Among the most important innovations, microarray technology allows to quantify the expression for thousand of genes simultaneously. The characteristic of these data which makes it different from machine-learning/pattern recognition data includes, a fair amount of random noise, missing values, a dimension in the range of thousands, and a sample size in few dozens. A particular application of the microarray technology is in the area of cancer research, where the goal is for precise and early detection of tumorous cells with high accuracy. The challenge for a biologist and computer scientist is to provide solution based on terms of automation, quality and efficiency.

In this thesis, comprehensive studies have been carried out on application of clustering techniques to machine learning data and bioinformatics data. Two sets of dataset have been considered in this thesis for the simulation study. The first set contains fifteen datasets with class-labeled information and second set contains three datasets without class-labeled information. Since the work carried out in this thesis is based on unsupervised classification (i.e., clustering); class-labeled information was not used while forming clusters. To validate clustering algorithm, for first set of data (i.e., data with

class-labeled information), clustering accuracy was used as cluster validation metric while for second set of data (i.e., data without class-labeled information), *HS_Ratio* was used as cluster validation metric. Considering machine learning data, studies have been made on Iris data and WBCD (Wisconsin Breast Cancer Data) and for bioinformatics data, studies have been done on microarray data. Varieties of microarray cancer data have been considered e.g., Breast Cancer, Leukemia Cancer, Lymphoma Cancer (DLBCL), Lung Cancer, Serum cancer etc. to assess the performance of clustering algorithm.

This thesis explores and evaluates Hard C-means (HCM) and Soft C-means (SCM) algorithm for machine learning data as well as bioinformatics data. Unlike HCM, SCM algorithm provides a presence of a gene in more than one cluster at a time with different degree of membership. Simulation studies have been carried out using datasets having class labeled information. Comparative studies have been made between results of Hard C-means and Soft C-means clustering algorithms.

In this thesis, a family of Genetic algorithm (GA) based clustering techniques have been studied. Problem representation is one of the key decision to be made when applying a GA to a problem. Problem representation under GA, determines the shape of the solution space that GA must search. As a result, *different encodings of the same problem are essentially different problems for a GA*. Four different type of encoding schemes for chromosome representation have been studied for supervised/un-supervised classification. The novelty of the algorithm lies with two factors i.e., 1) proposition of new encoding schemes and, 2) application of novel fitness function (HS_Ratio). Simulation studies have been carried out using dataset having class labeled information. Extensive computer simulation shows that GA based clustering algorithm was able to provide the highest accuracy and generalization of results compared to Non-GA based clustering Algorithm.

In this thesis, a Brute-Force method was also proposed for clustering. Simulation studies have been carried out using datasets without class labeled information. Advantage of the proposed approach is that it is computationally faster compared to conventional HCM clustering algorithm and thus it could be useful for high dimensional bioinformatics data. Unlike HCM, the proposed Brute-Force clustering algorithm does not require number of cluster "*C*" from the user and thus provides automation.

A Simulated Annealing (SA) based preprocessing method was also proposed for data diversification. Simulation studies have been carried out using dataset without class labeled information. Extensive simulation on real and artificial data shows that HCM algorithm with SA based preprocessing performs superior compared to conventional HCM clustering algorithm.

Comprehensive study has also been taken up for cluster validation metrics for several clustering algorithms. For gene expression data, clustering results in groups of co-expressed genes (gene based clustering), groups of samples with a common phenotype (sample based clustering), or "*blocks*" of genes and samples involved in specific biological processes (subspace clustering). However, different clustering validation parameter, generally result in different sets of clusters. Therefore, it is important to compare various cluster validation metrics and select the one that fits best with the "*true*" data distribution. Cluster validation is the process of assessing the quality and reliability of the cluster sets derived from various clustering processes. A comparative study has been done on three cluster validation metrics namely, HS_Ratio, Figure oF Merit (FOM) and cluster Accuracy for assessing the quality of different clustering algorithm.

List of Acronyms

Acronym	Description
BF	Brute Force
FCM	Fuzzy C-Means
FOM	Figure of Merit
GA	Genetic Algorithm
$GA-R1$	Genetic Algorithm Representation 1
$GA-R2$	Genetic Algorithm Representation 2
$GA-R3$	Genetic Algorithm Representation 3
HCM	Hard C-Means
HS_Ratio	Homogeneity to Separation Ratio
KDD	Knowledge Discovery in Databases
$NCBI$	National Center for Biotechnology Information
SA	Simulated Annealing
SCM	Soft C-Means

List of Symbols

Symbol	Description
S	Datasets
n	Number of Data point
N	Number of Dimension
C	Number of Cluster
V	Set of clusters
V_j	j^{th} Cluster
v_j	Center of j^{th} Cluster
v_j^*	Center of j^{th} Cluster after updation
m	Fuzziness parameter
$\mu V_j(x)$	Membership of x in cluster V_j
U_{ij}	Membership of gene ‘i’ in cluster ‘j’
$x \in V_j$	x is member of V_j
P	Size of population
P_c	Cross-over probability
cp	Cross-over point
cs	Size of chromosome
p_m	Mutation probability
E_i	i^{th} gene
D	Distance matrix
D_{ij}	Distance between gene ‘i’ and gene ‘j’
θ	Thresold value for Brute-Force
ε	Thresold value for SCM
J	Fitness function
$\parallel V \parallel$	Cardinality of cluster ‘V’

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Chapter 1

Introduction

The most important characteristic of the information age is the knowledge discovery from the huge pool of abundant data. Advances in computer technology, in particular the Internet, have led to "data explosion". Of late, the aspect of data availability has been increased much more than assimilation capacity of any normal human being. According to a recent study conducted at UC Berkeley, the amount of generated data have grown exponentially in last one decade [1]. This increase in both the volume and the variety of data calls for advances in methodology to understand, process, and summarize the data. From a more technical point of view, understanding the structure of large data sets arising from the data explosion is of fundamental importance in data mining, pattern recognition, and machine learning. In this thesis work, focus has been given on data mining techniques particularly clustering for data analysis in machine learning as well as in bioinformatics. The characteristic of bioinformatics data which makes it different from machine-learning data includes, a fair amount of random noise, missing values, a dimension in the range of thousands, and a sample size in few dozens.

1.1 Data Analysis

The word "data", as simple as it seems, is not easy to define precisely. In this thesis, a pattern recognition perspective has been considered for data and it defines the data as the description of "*a set of objects or patterns*" that can be processed by a computing system. The objects are assumed to have some commonalities, so that the same systematic procedure can be applied to all the objects to generate the description.

1.1.1 Types of Data

Data can be classified into different types. Most often, an object is represented by the results of measurement of its various properties [2]. A measurement result is called a " *feature*" in pattern recognition or "a variable" in statistics. The concatenation of all the features of a single object forms the ***feature vector***. By arranging the feature vectors of different objects in different rows, a pattern matrix (also called "data matrix") of size "n" by "N" is obtained, where "n" is the total number of objects and "N" is the number of features. This representation is very popular because it converts different kinds of objects into a standard representation. If all the features are numerical, an object can be represented as a point in R^N. This enables a number of mathematical tools which can be used to analyze the objects.

1.1.2 Types of Features

The feature vector representation, descriptions of an object can be classified into different types [3]. A feature is essentially a measurement, and the "scale of measurement" can be used to classify features into different categories. They are:

- Nominal: discrete, unordered. Examples: "apple", "orange", and "banana".
- Ordinal: discrete, ordered. Examples: "conservative", "moderate", and "liberal".
- Interval: continuous, no absolute zero can be negative. Examples: temperature in Fahrenheit.
- Ratio: continuous, with absolute zero, positive. Examples: length, weight.
- Numerical: continuous, with positive, zero and negative values.

In this thesis, studies have been made on microarray data which are numerical in nature.

1.1.3 Types of Analysis

The analysis to be performed on the data can be classified into different types [4]. It can be exploratory/descriptive, meaning that the investigator does not have a specific goal and only wants to understand the general characteristics or structure of the data. It can be confirmatory/inferential, meaning that the investigator wants to confirm the validity of a hypothesis/model or a set of assumptions using the available data. In pattern recognition, most of the data analysis is concerned with predictive modeling: given some existing data ("training data"), goal is to predict the behavior of the unseen data ("testing data"). This is often called "machine learning" or simply "learning." Depending on the type of feedback one can get in the learning process, three types of learning techniques have been suggested [2]. In supervised learning, labels on data points are available to indicate if the prediction is correct or not. In un-supervised learning, such label information is missing. In reinforcement learning, only the feedback after a sequence of actions that can change the possibly unknown state of the system is given. In the past few years, a hybrid learning scenario between supervised and un-supervised learning, known as semi-supervised learning, transductive learning [5], or learning with unlabeled data [6], has been emerged, where only some of the data points have labels. This scenario happens frequently in bioinformatics applications, since data collection and feature extraction can often be automated, whereas the labeling of patterns or objects has to be done manually, but this job is expensive both in time and cost.

In this thesis, work has been carried out on un-supervised classification i.e., Clustering to investigate the hidden pattern available in machine learning data as well as bioinformatics data.

1.2 Data Mining and Knowledge Discovery

With the enormous amount of data stored in files, databases, and other repositories, it is increasingly important, to develop powerful means for analysis and perhaps interpretation of such data and for the extraction of interesting knowledge that could help in decision-making. Data Mining, also popularly known as Knowledge Discovery in Databases (KDD), refers to as "the nontrivial process of identifying valid, novel, potentially useful and ultimately understandable pattern in data". While data mining and knowledge discovery in databases (KDD) are frequently treated as synonyms, data mining is actually part of the knowledge discovery process. Figure 1.1 shows data mining as a step in an iterative knowledge discovery process. The task of the knowledge discovery and data mining process is to extract knowledge from data such that the resulting knowledge is useful in a given application. The Knowledge Discovery process in Databases comprises of a few steps leading from raw data collections to some form of retrieving new knowledge. The iterative process consists of the following steps:

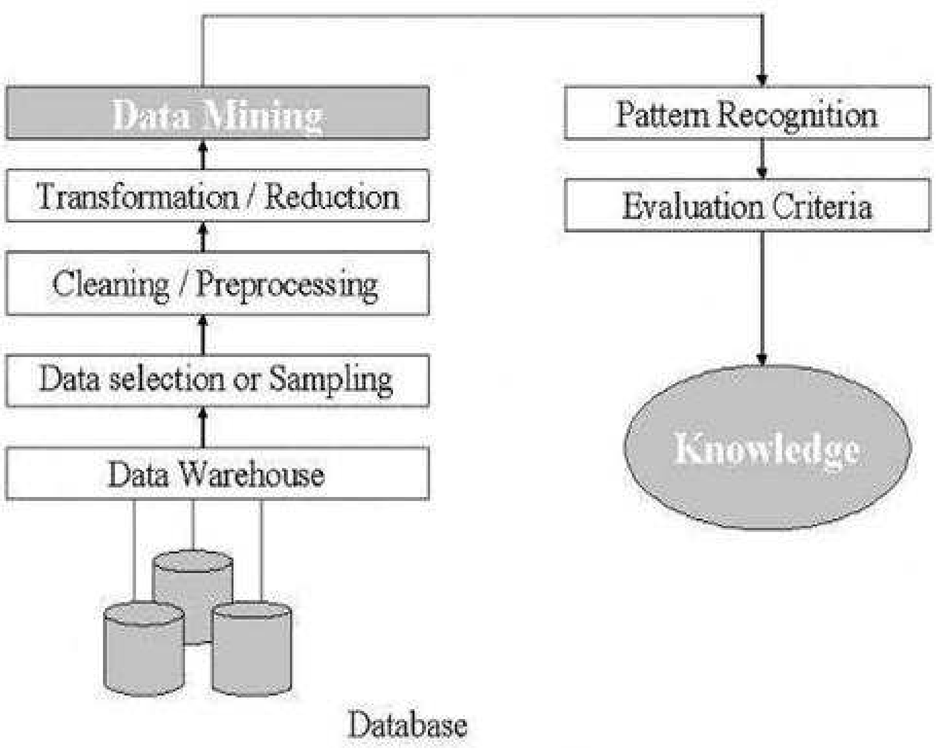


Figure 1.1: Complete Overview of Knowledge discovery from Databases

- Data cleaning: Also known as data cleansing, it is a phase in which noisy data and irrelevant data are removed from the collection.
- Data integration: At this stage, multiple data sources, often heterogeneous, may be combined in a common source.
- Data selection: At this step, the data relevant to the analysis is decided on and retrieved from the data collection.
- Data mining: It is the crucial step in which clever techniques are applied to extract data patterns potentially useful.

- Pattern evaluation: In this step, strictly interesting patterns representing Knowledge is identified based on given measures.
- Knowledge representation: Is the final phase in which the discovered knowledge is visually represented to the user. This essential step uses visualization techniques to help users understand and interpret the data mining results.

It is common practice to combine some of steps together for specific application. For instance, data cleaning and data integration can be performed together as a pre-processing phase to generate a data warehouse (1.1). Data selection and data transformation can also be combined where the consolidation of the data is the result of the selection, or, as for the case of data warehouses, the selection is done on transformed data. The KDD is an iterative process. Once the discovered knowledge is presented to the user, the evaluation measures can be enhanced, the mining can be further refined, new data can be selected or further transformed, or new data sources can be integrated, in order to get different, more appropriate results.

1.3 Data Mining Models

There are several data mining models, some of these are narrated below which are conceived to be important in the area of "Data Mining" [7], [8].

- Clustering: It segments a large set of data into subsets or clusters. Each cluster is a collection of data objects that are similar to one another with the same cluster but dissimilar to object in other clusters [7], [8], [9], [10], [11].
- Classification: Decision trees, also known as classification trees, are a statistical tool that partitions a set of records into disjunctive classes. The records are given as tuples with several numerics and categorical attributes with one additional attribute being the class to predict. Decision trees algorithm differs in selection of variables to split and how they pick the splitting point [7], [8].
- Association Mining: It uncovers interesting correlation patterns among a large set of data items by showing attribute value conditions that occur together frequently [7], [8].

1.4 Application of Data mining

Data mining has become an important area of research since last decade. Important area where Data mining can be effectively applied are as follows: Health sector (Biology/Bioinformatics), Image Processing(Image segmentation), Ad-Hoc wireless Network(clustering of nodes), Intrusion detection system, Finance sector etc.
In this thesis focus has been given on clustering techniques and their application to machine learning and bioinformatics data.

1.5 Motivation

A number of clustering methods have been studied in the literature; they are not satisfactory in terms of: 1) automation, 2) quality, and 3) efficiency.

- With regard to automation, most clustering algorithms request users to input some parameters needed to conduct the clustering task. For example, Hard C-means clustering algorithm ([7], [8], [9], [10], [11]) requires the user to input the number of clusters "C" to be generated. However, in real life applications, it is often difficult to predict the correct value of '*C*'. Hence, an automated clustering method is required.

- As for quality, an accurate validation method for evaluating the quality of clustering results is lacking. Consequently, it is difficult to provide the user with information regarding how good each clustering result is.

- As for efficiency, the existing clustering algorithms(e.g., Hard C-means) may not perform well when the optimal or near-optimal clustering result is required from the global point of view.

1.6 Objective

Based on the motivation outlined in the previous section, the main objective of the study is clustering of gene expression data i.e., to group genes based on similar expressions over all the conditions. That is, genes with similar corresponding vectors should be classified into the same cluster. More specifically, the main objectives of the study is as follows:

- For cluster formation; C-means algorithm (Hard C-means) [7], [8], [9], [10], [11] to machine intelligence data as well as to various bioinformatics data (Gene expression microarray cancer data) and to assess the effectiveness of the algorithm has been studied.
- To apply soft C-means algorithm (or, Fuzzy C-Means, FCM) ([7], [8], [9], [10], [11] to same data and to explore how its helps in fuzzy partition of the data (i.e. how it intends to accommodate one gene to two different clusters at same time with different degree of membership).
- To propose family of Genetic Algorithm based clustering techniques for multivariate data. Four different types of encoding schemes for clustering has been studied.
- Lastly, a Brute-Force incremental approach for clustering and a Simulated Annealing (SA) [12] based method for diversification of the data has been proposed.
- To assess the performance of the proposed model; three Clustering Validation metrics : Clustering accuracy, HS_Ratio [13] and Figure of Merit (FOM [13]) have been considered.

1.7 Organization of the Thesis

The contents of the thesis is organized as follows:

Chapter 2 discusses the background concepts used in the thesis. First, discussion has been made on bioinformatics and after that application of clustering to gene expression microarray data.

Chapter 3 provides a brief review of related work on microarray data and clustering techniques. Emphasis has been given on research work reported in literature in context to HCM, SCM and Genetic algorithm based clustering algorithm and their application to pattern recognition data (machine learning data) and gene expression bioinformatics data.

Chapter 4 presents comparative study on conventional Hard C-means clustering algorithm and Soft C-means clustering. In this chapter, initially discussion has been made on basic steps involved in Hard C-means and Soft C-means clustering algorithm and then their application to several machine learning data as well as bioinformatics data.

Chapter 5 presents Family of Genetic algorithm based clustering algorithm. In this chapter, first, discussion has been made on basic steps involved in GA based clustering. Next, discussion has been carried out on four novel methods for representing a chromosome and HS_Ratio ratio as fitness function for evaluation of fitness of a chromosome. Later discussion has been made on application of GA based clustering algorithm to machine learning data and bioinformatics data.

Chapter 6 presents an incremental Brute-Force based clustering method and Simulated Annealing based method for diversification of the data.

Chapter 7 presents comparative studies on several cluster validation matrices for assessing the goodness of a clustering algorithm.

Chapter 8 presents the conclusion about work done in this thesis.

Chapter 2

Background Concepts

This chapter discusses background concepts, definitions, and notations on bioinformatics and clustering, that are used throughout the thesis.

2.1 Bioinformatics

Bioinformatics ([13], [14], [15], [16]) is the application of information technology to the field of molecular biology. The term bioinformatics was coined by Paulien Hogeweg in 1978 for the study of informatics processes in biotic systems. The National Center for Biotechnology Information (NCBI, 2001) defines bioinformatics as "the field of science in which biology, computer science, and information technology merges into a single discipline". There are three important area in bioinformatics: 1.) the development of new algorithms and statistics with which to assess relationships among members of large data sets; 2.) the analysis and interpretation of various types of data including nucleotide and amino acid sequences, protein domains, and protein structures; 3.) and the development and implementation of tools that enable efficient access and management of different types of information. The explosive growth in the amount of biological data demands the use of computing systems for the organization, the maintenance and the analysis of biological data. The aims of bioinformatics are:

1. The organization of data in such a way that allows researchers to access existing information and to submit new entries as they are produced.

2. The development of tools that help in the analysis of data.

3. The use of these tools to analyze the individual systems in detail, in order to gain new biological insights.

In this thesis, work will be focused on the development of tools that help in the analysis of data.

2.1.1 Application of Data Mining techniques to Bioinformatics

There are several sub areas in bioinformatics where Data mining can be effectively use for finding useful information from the biological data [13], [14]. Some of the areas are described below in brief:

- Data mining in Gene Expression: Gene expression analysis is the use of quantitative mRNA-level measurements of gene expression (the process by which a gene's coded information is converted into the structural and functional units of a cell) in order to characterize biological processes and elucidate the mechanisms of gene transcription [13].

- Data mining in genomics: Genomics is the study of an organism's genome and deals with the systematic use of genome information to provide new biological knowledge ([14]).

- Data Mining in Proteomics: Proteomics is the large-scale study of proteins. Data mining can be used particularly for prediction of protien's structures and functions [16].

As far as this thesis is concerned, the main area of focus is application of data mining techniques to gene expression analysis. In next section, microarray technology has been described for gene expression data.

2.1.2 Introduction to Microarray Technology

Compared with the traditional approach to genomic research, which is focused on the local examination and collection of data on single genes, microarray technologies have now made it possible to monitor the expression levels for tens of thousands of genes in parallel. The two major types of microarray experiments are the cDNA microarray and oligonucleotide arrays (abbreviated oligo chip). Despite differences in the details of their experiment protocols, both types of experiments involve three common basic procedures ([13], [14], [15]) :

1. Chip manufacture: A microarray is a small chip (made of chemically coated glass, nylon membrane or silicon), onto which tens of thousands of DNA molecules (probes) are attached in fixed grids. Each grid cell relates to a DNA sequence.

2. Target preparation, labeling and hybridization: Typically, two mRNA samples (a test sample and a control sample) are reverse-transcribed into cDNA (targets), labeled using either fluorescent dyes or radioactive isotopic, and then hybridized with the probes on the surface of the chip.

3. The scanning process: Chips are scanned to read the signal intensity that is emitted from the labeled and hybridized targets.

Generally, both cDNA microarray and oligo chip experiments measure the expression level for each DNA sequence by the ratio of signal intensity between the test sample and the control sample, therefore, data sets resulting from both methods share the same biological semantics. In this thesis work, unless explicitly stated, gene expression data generated by both the cDNA microarray and the oligo chip as microarray technology are similar in nature.

2.1.3 Gene Expression Data

A microarray experiment [15] typically assesses a large number of DNA sequences (genes, cDNA clones, or expressed sequence tags) under multiple conditions. These conditions may be a time series during a biological process or a collection of different tissue samples (e.g., normal versus cancerous tissues). In this thesis work, studies have been carried out on both time series as well as tissue sample microarray data. A gene expression data set [13] from a microarray experiment can be represented by a real-valued expression matrix $E = \left\{E_{ij} \mid 1 \leq i \leq n, 1 \leq j \leq N\right\}$ as shown in fig. 2.2, where the row forms the expression patterns of genes, the columns represent the expression profiles of samples, and each cell is the measured expression level of gene 'i' in sample 'j'.

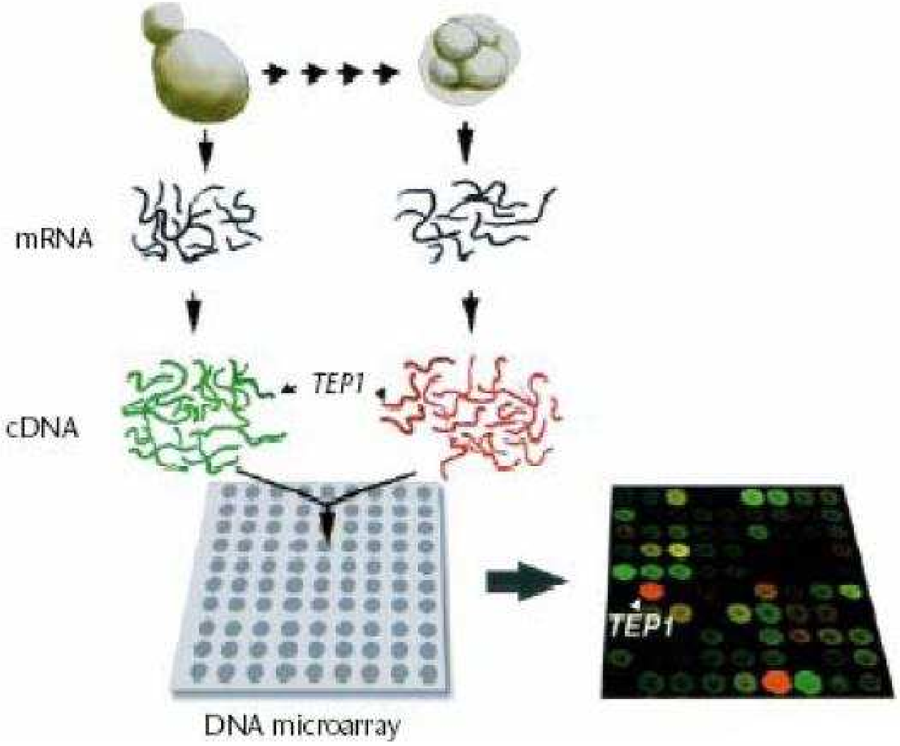
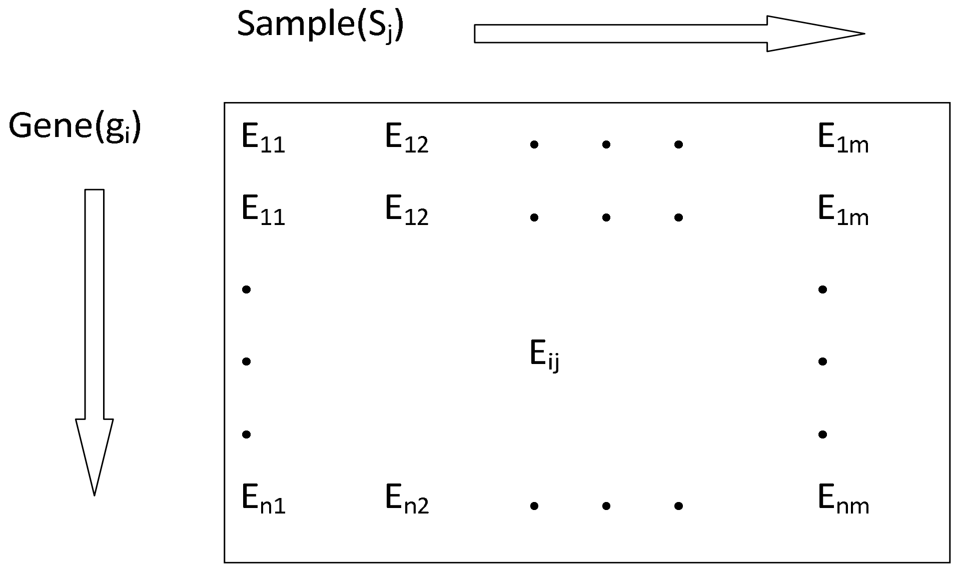


Figure 2.1: Microarray Technology: Overview of gene expression analysis using a DNA microarray. (**Source**: P. O. Brown & D. Botstein, Nat. Genet, Vol. 21, No. 1, pp. 33-37, January 1999)

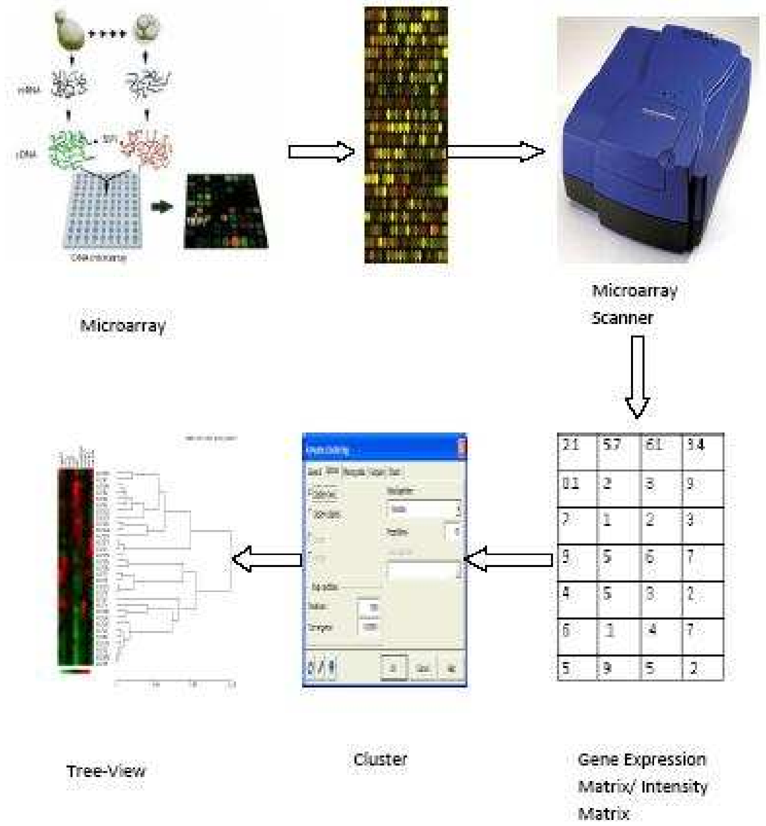
2.2 Clustering

Clustering [7], [8], [9], [10], [11] is the process of grouping data objects into a set of disjoint classes, called clusters, so that "*objects within the same class have high similarity to each other, while objects in separate classes are more dissimilar*". Clustering is an example of un-supervised classification. "Classification" refers to a procedure that assigns data objects to a set of predefined classes. "Un-supervised" means that clustering does not rely on predefined classes and training examples while classifying the data objects. Thus, clustering is distinguished from pattern recognition or the areas of statistics known as discriminate analysis and decision analysis, which seek to find rules for classifying objects from a given set of pre-classified objects.



$$\begin{array}{cccccc}
E_{11} & E_{12} & \bullet & \bullet & \bullet & E_{1m} \\
E_{11} & E_{12} & \bullet & \bullet & \bullet & E_{1m} \\
\bullet & & & & & \bullet \\
\bullet & & E_{ij} & & & \bullet \\
\bullet & & & & & \bullet \\
E_{n1} & E_{n2} & \bullet & \bullet & \bullet & E_{nm}
\end{array}$$

Figure 2.2: Gene Expression Matrix/Intensity Matrix



21	57	61	34
01	2	3	9
7	1	2	3
9	5	6	7
4	5	3	2
6	1	4	7
5	9	5	2

Figure 2.3: Complete Overview of Gene Expression Analysis

2.2.1 Formal Definition of Clustering

The clustering problem is defined as the problem of classifying ‘n’ objects into ‘C’ clusters without any apriori knowledge [17]. Let the set of ‘n’ points be represented by the set ‘S’ and the ‘C’ clusters be represented by $V_1, V_2, \ldots, V_C$. Then

$$
\begin{gathered}
V_i \neq \emptyset \text{ for } i = 1, 2, \ldots, C, \\
V_i \bigcap V_j = \emptyset \text{ for } i = 1, 2, \ldots, C \text{ and } i \neq j \\
\text{and } \cup_{i=1}^{C} V_i = S
\end{gathered}
$$

2.2.2 Categories of Gene Expression Data Clustering

Typically, microarray experiment contains 10^3 to 10^4 genes, and this number is expected to reach the order of 10^6. However, the number of samples involved in microarray experiment is generally in the order of 10^2. One of the characteristics of gene expression data is that it is meaningful to cluster both genes and samples. Clustering gene expression data can be categorized into three groups [13].

1. **Gene based clustering :** In this type of clustering genes are treated as the objects, while samples as the features. The purpose of gene-based clustering is to group together co-expressed genes which indicate co-function and co-regulation. Example of gene-based clustering which have been used in literature are K-means [18], SOM [19], CLICK [20], DHC [21], CAST [22], agglomerative hierarchical [23], model-based clustering [24] etc.

2. **Sample based clustering:** In this type of clustering samples are the objects and genes are features. Within a gene expression matrix, there are usually particular macroscopic phenotype of samples related to some diseases or drug effects, such as diseased samples, normal samples or drug treated samples. The goal of sample based clustering is to find the phenotype structures or sub-structures of the sample. Example of sample-based clustering which have been used in literature are Xing et. al. [25], Ding. et. al. [26], Hastie et.al. [27], Tang et. al. [28], [29] etc.

3. **Subspace Clustering:** In this type of clustering, job is to find subsets of objects such that the objects appear as a cluster in a subspace formed by a subset of the

features. In subspace clustering, the subsets of features for various subspace clusters can be different. Two subspace clusters can share some common objects and features, and some objects may not belong to any subspace cluster. Example of subspace clustering which have been used in literature are CTWC [30], Biclustering [31], δ $-$ cluster [32], plaid model [33] etc. .

2.2.3 Proximity measurement for Gene Expression Data

Proximity measurement [13] measures the similarity (or, dissimilarity) between two data objects. Gene expression data objects, no matter genes or samples, can be formalized as numerical vectors $E_i = \{E_{i,j} \mid 1 \leq j \leq N\}$, where $E_{i,j}$ is the value of the j^{th} feature for the i^{th} data object and N is the number of features. The proximity between two objects E_i and E_j is measured by a proximity function of corresponding vectors. There are several proximity measures available in literature like Euclidean Distance, Pearson correlation coefficient, Jackknife correlation, spearman's rank-order correlation coefficient etc. A useful review on proximity measurement can be found reference [7], [8], [9], [10], [11], [13]. Among these all proximity measures, Euclidean Distance is the simplest one and easy to implement.

2.2.4 Euclidean Distance

Euclidean Distance is one of the most commonly used methods to measure the distance between two data objects. The distance between objects E_i and E_j in N-dimensional space is defined as:

$Euclidean(E_i, E_j) = \sqrt{\sum_{k=1}^{N} \left(E_{ik} - E_{jk}\right)^2}$

Euclidean distance does not score well for shifting or scaled patterns (or profiles). To address this problem, each object vector is standardized with zero mean and variance one before calculating the distance [7], [8].

In next chapter, discussion has been made on literature work carried out on microarray data and clustering techniques.

Chapter 3

Review of Related Work

This chapter provides overview of research carried out on clustering algorithm and their application to several microarray data reported in literature. This chapter is broadly divided into two section. First section deals with research work carried out on several microarray data and section two deals with research carried out on different clustering algorithm

3.1 Review work carried out on Microarray data

DNA microarrays are high-throughput methods for analyzing complex nucleic acid samples. It makes possible to measure rapidly, efficiently and accurately the levels of expression of all genes present in a biological sample. The application of such methods in diverse experimental conditions generates lots of data. However, the main problem with these data occurs while analyzing it. Derivation of meaningful biological information from raw microarray data is impeded by the complexity and vastness of the data [34]. To overcome the problem associated with gene expression microarray data many statistical methods has been proposed in recent past. Some important has been explained below:

- Eisen, Spellman, Brown and Botstein (1998) [23]: The paper deals with study on Hierarchical clustering of gene expression data of budding yeast Saccharomyces cerevisiae and human gene data. The paper claims that clustering of budding yeast Saccharomyces cerevisiae gene expression data groups together efficiently genes of known similar function, and similar tendency were also obtained in human data. Thus patterns seen in genome-wide expression experiments can be interpreted as indications of the status of cellular processes. Also, co-expression of genes of known function with poorly characterized or novel genes may provide a simple means of gaining leads to the functions of many genes for which information is not available currently.

- Tamayo, Slonim, Mesirov, Zhu, Kitaeewan and Dmitrovsky (1999) [19]: This paper describes the application of self-organizing maps, a type of mathematical cluster analysis that is particularly well suited for recognizing and classifying features in complex, multidimensional data. The method has been implemented in a publicly available computer package, GENECLUSTER, that performs the analytical calculations and provides easy data visualization. To illustrate the value of such analysis, the approach is applied to hematopoietic differentiation in four well studied models (HL-60, U937, Jurkat, and NB4 cells). Expression patterns of some 6,000 human genes were assayed, and an online database was created. GENECLUSTER was used to organize the genes into biologically relevant clusters that suggest novel hypotheses about hematopoietic differentiation. For example, highlighting certain genes and pathways involved in 'differentiation therapy' used in the treatment of acute promyelocytic leukemia.

- Iyer, Eisen, Ross, Schuler, Moore, Lee, Trent, Hudson, Boguski, Lashkari, Bostein, and Brown (1999) [35]: The paper deals with temporal program of gene expression during a model physiological response of human cells, the response of fibroblasts to serum, was explored with a complementary DNA microarray representing about 8600 different human genes. Genes could be clustered into groups on the basis of their temporal patterns of expression in this program. Many features of the transcriptional program appeared to be related to the physiology of wound repair, suggesting that fibroblasts play a larger and richer role in this complex multicellular response than had previously been appreciated.

- Chu, Eisen, Mulholland, Botstein, Brown and Herskowitz (1998) [36]: The paper deals with developmental program of sporulation of budding yeast. Diploid cells of budding yeast produce haploid cells through the developmental program of sporulation, which consists of meiosis and spore morphogenesis. DNA microarrays containing nearly every yeast gene were used to assay changes in gene expression during sporulation. At least seven distinct temporal patterns of induction were observed. The transcription factor Ndt80 appeared to be important for induction of a large group of genes at the end of meiotic prophase. Consensus sequences known or proposed to be responsible for temporal regulation could be identified solely from analysis of sequences of coordinately expressed genes. The temporal expression pattern provided clues to potential functions of hundreds of previously uncharacterized genes, some of which have vertebrate homologs that may function during gametogenesis.

- Spellman, Sherlock, Iyer, Zhang, Anders, Eisen, Brown and Bostein (1998) [37] : This paper creates a comprehensive catalog of yeast genes whose transcript levels vary periodically within the cell cycle. To this end, DNA microarrays have been used and samples from yeast cultures synchronized by three independent methods: alpha factor arrest, elutriation, and arrest of a cdc15 temperature-sensitive mutant. Using periodicity and correlation algorithms, 800 genes were identified that meet an objective minimum criterion for cell cycle regulation. In separate experiments, designed to examine the effects of inducing either the G1 cyclin Cln3p or the B-type cyclin Clb2p, It was found that the mRNA levels of more than half of these 800 genes respond to one or both of these cyclins. Furthermore, analysis was done on set of cell cycle-regulated genes for known and new promoter elements and show that several known elements (or variations thereof) contain information predictive of cell cycle regulation.

- Roth, Estep, and Church (1998) [38] :In this paper Whole-genome mRNA quantitation was used to identify the genes that are most responsive to environmental or genotypic change. By searching for mutually similar DNA elements among the upstream non-coding DNA sequences of these genes, identification of candidate regulatory motifs and corresponding candidate sets of co-regulated genes can be made. This strategy was tested by applying it to three extensively studied regulatory systems in the yeast Saccharomyces cerevisiae: galactose response, heat shock, and mating type. Galactose-response data yielded the known binding site of Gal4, and six of nine genes known to be induced by galactose. Heat shock data yielded the cell-cycle activation motif, which is known to mediate cell-cycle dependent activation, and a set of genes coding for all four nucleosomal proteins. Mating type alpha and a data yielded all of the four relevant DNA motifs and most of the known a and alpha-specific genes.

- Cho R. J., Campbell M. J., Winzeler E. A., Steinmetz L., Conway A., Wodicka L., Wolfsberg T. G., Gabrielian A. E., Landsman D., Lockhart D. J., Davis R.W. (1998) [39]: The paper deals with the genome-wide characterization of mRNA transcript levels during the cell cycle of the budding yeast S. cerevisiae. Cell cycle-dependent periodicity was found for 416 of the 6220 monitored transcripts. More than 25 % of the 416 genes were found directly adjacent to other genes in the genome that displayed induction in the same cell cycle phase, suggesting a mechanism for local chromosomal organization in global mRNA regulation. More than 60 % of the characterized genes that displayed mRNA fluctuation have already been implicated in cell cycle period-specific biological roles. Because more than 20 % of human proteins display significant homology to yeast proteins, these results also link a range of human genes to cell cycle period-specific biological functions.

- Bhattacharjee A., Richards WG, Staunton J, Li C, Monti S, Vasa P, Ladd C, Beheshti J,Bueno R, Gillette M, Loda M, Weber G, Mark EJ, Lander ES, Wong W, Johnson BE, Golub TR, Sugarbaker DJ, Meyerson M.(2001) [40]: In this paper a molecular taxonomy of lung carcinoma has been generated. Using oligonucleotide microarrays, analysis was made on mRNA expression levels corresponding to 12,600 transcript sequences in 186 lung tumor samples, including 139 adenocarcinomas resected from the lung. Hierarchical and probabilistic clustering of expression data defined distinct subclasses of lung adenocarcinoma. Among these were tumors with high relative expression of neuroendocrine genes and of type II pneumocyte genes, respectively. Retrospective analysis revealed a less favorable outcome for the adenocarcinomas with neuroendocrine gene expression.

The diagnostic potential of expression profiling is emphasized by its ability to discriminate primary lung adenocarcinomas from metastases of extra-pulmonary origin. The results shown in paper suggest that integration of expression profile data with clinical parameters could aid in diagnosis of lung cancer patients.

- Golub T. R., Slonim D. K. , Tamayo P., Huard C., Gaasenbeek M., Mesirov J. P., Coller H., Loh M. L. , Downing J. R., Caligiuri M. A., Bloomfield C. D., Lander E. S. (1999) [41]: In this paper, a generic approach to cancer classification based on gene expression monitoring by DNA microarrays was described and applied to human acute leukemias as a test case. A class discovery procedure automatically discovered the distinction between acute myeloid leukemia (AML) and acute lymphoblastic leukemia (ALL) without previous knowledge of these classes. An automatically derived class predictor was able to determine the class of new leukemia cases. The results demonstrate the feasibility of cancer classification based solely on gene expression monitoring and suggest a general strategy for discovering and predicting cancer classes for other types of cancer, independent of previous biological knowledge.

- Laura J., Van ’t veer [42]: The paper deals with Breast cancer microarray data. Breast cancer patients with the same stage of disease can have markedly different treatment responses and overall outcome. The strongest predictors for metastases (for example, lymph node status and histological grade) fail to classify accurately breast tumours according to their clinical behaviour. Chemotherapy or hormonal therapy reduces the risk of distant metastases by approximately one-third; however, 70-80 % of patients receiving this treatment would have survived without it. None of the signatures of breast cancer gene expression reported to date allow for patient-tailored therapy strategies. In the paper, DNA microarray analysis on primary breast tumours of 117 young patients has been carried out, and applied supervised classification to identify a gene expression signature strongly predictive of a short interval to distant metastases (‘poor prognosis’ signature) in patients without tumour cells in local lymph nodes at diagnosis (lymph node negative). In addition, a signature that identifies tumours of BRCA1 carriers has been established. The poor prognosis signature consists of genes regulating cell cycle, invasion, metastasis and angiogenesis. This gene expression profile outperforms all currently used clinical parameters in predicting disease outcome.

- West M., Blanchette C., Dressman H., Huang E., Ishida S., Spang R., Zuzan H., Olson J. A. Jr., Marks J. R., Nevins J. R. (2001) [43]: In this paper, Bayesian regression models has been developed that provide predictive capability based on gene expression data derived from DNA microarray analysis of a series of primary breast cancer samples. These patterns have the capacity to discriminate breast tumors on the basis of estrogen receptor status and also on the categorized lymph node status. Importantly, in the paper assessment was done on the utility and validity of such models in predicting the status of tumors in cross-validation determinations. The practical value of such approaches relies on the ability not only to assess relative probabilities of clinical outcomes for future samples but also to provide an honest assessment of the uncertainties associated with such predictive classifications on the basis of the selection of gene subsets for each validation analysis. This latter point is of critical importance in the ability to apply these methodologies to clinical assessment of tumor phenotype.

- Shipp M. A., Ross K. N., Tamayo P., Weng A.P., Kutok J. L., Aguiar R. C., Gaasenbeek M., Angelo M., Reich M., Pinkus G. S., Ray T. S., Koval M. A., Last K. W., Norton A., Lister T. A., Mesirov J.,Neuberg D. S., Lander E. S., Aster J. C., Golub T. R. (2002) [44]: Diffuse large B-cell lymphoma (DLBCL), the most common lymphoid malignancy in adults, is curable in less than 50 % of patients. Prognostic models based on pre-treatment characteristics, such as the International Prognostic Index (IPI), are currently used to predict outcome in DLBCL. However, clinical outcome models identify neither the molecular basis of clinical heterogeneity, nor specific therapeutic targets. In this paper analysis has been done on the expression of 6,817 genes in diagnostic tumor specimens from DLBCL patients who received cyclophosphamide, adriamycin, vincristine and prednisone (CHOP)-based chemotherapy, and applied a supervised learning prediction method to identify cured versus fatal or refractory disease. The algorithm classified two categories of patients with very different five-year overall survival rates (70% versus 12%). The model also effectively delineated patients within specific IPI risk categories who were likely to be cured or to die of their disease. Genes implicated in DLBCL outcome included some that regulate responses to B-cell-receptor signaling, critical serine/threonine phosphorylation pathways and apoptosis. Result shown in paper indicates that supervised learning classification techniques can predict outcome in DLBCL and identify rational targets for intervention.

3.2 Review on Clustering algorithm

Lots of work has been done in clustering in recent past. A useful review on clustering can be found out from the following referenced paper [7], [8], [9], [10], [13], [34], [45], [46]. In this section, discussion has been made on various work done in literature on HCM, SCM and GA based clustering.

3.2.1 Review on Hard C-means Clustering Algorithm

The Hard C-means clustering (HCM) algorithm is one of the best-known squared error-based clustering algorithm [7], [8], [9], [10]. It is very simple and can be easily implemented in solving many practical problems. It can work very well for compact and hyper-spherical clusters. The time complexity of Hard C-means is '$O(n \times C \times N)$' and space complexity is '$O(n + C)$', where 'n' is number of data points, 'N' is number of feature and 'C' is number of cluster in consideration. Since 'C' and 'N' are usually much less than 'n', Hard C-means can be used to cluster large data sets in least time.
The HCM algorithm has been extensively applied in several areas [7], [8], [9], [10]. HCM algorithm has been extensively studied in the past for its applicability to pattern recognition and machine learning data. Application of HCM to Iris data has been reported in paper [47], [48], [49], [46]. The number of wrongly clustered instances in case of Iris may vary from 14 to 17 [47]. HCM has also been used in recent past in case of WBCD [46]. Application of HCM clustering algorithm to microarray gene expression analysis has been also reported in literature [18], [50]. Herwig et. al. developed a variant of HCM algorithm and applied to cluster a set of 2029 human cDNA clones

and adopted mutual information as the similarity measure [50]. Tavazoie et al. partitioned 3 000 genes into 30 clusters with the HCM algorithm [18]. For each cluster, 600 base pairs upstream sequences of the genes were searched for potential motifs. 18 motifs were found from 12 clusters in their experiments and 7 of them can be verified according to previous empirical results in the literature. A more comprehensive investigation can be found in [18]. Application of HCM algorithm to DNA or protein sequences clustering has been reported in paper [51]. In paper [51], protein or DNA sequences were transformed into a new feature space based on the detected sub-patterns and subsequently clustered with the HCM algorithm [51].

The drawbacks of HCM are also well studied in literature. Some of the major disadvantages are as follows:

1. There is no efficient and universal method for identifying the initial partitions in Hard C-means clustering algorithm. The convergence centroids vary with different initial points and that may results in suboptimal solution. This particular limitation of Hard C-means clustering algorithm has been extensively studied in literature such as [11], [52], [53], [54], [55], [56], [57], [58], [59], [60], [61], [62], [63], [64]. This problem is still an open issue of research.

2. The iteratively optimal procedure of Hard C-means cannot guarantee convergence to a global optimum. This particular problem was addressed in following paper: [65], [66], [67], [64], [12] The stochastic optimal techniques, like simulated annealing (SA), tabu search and genetic algorithms can be clubbed with Hard C-means to find the global optimum [9], [10].

3. Hard C-means algorithm is also sensitive to outliers and noise. Even if an object is quite far away from the cluster centroid, it is still forced into a cluster and, thus, distorts the cluster shapes [55], [11], [68].

4. The Hard C-means algorithm is limited to numerical variables [55], [68], [69], [70].

5. Determining the optimal number of clusters in a set of data is prerequisite to Hard

C-means clustering algorithm [55], [71], [72], [73], [74], [75], [76], [77], [78], [79], [80], [81], [82]

3.2.2 Review on Soft C-means based Clustering Algorithm

Soft C-means is a generalization of Hard C-means clustering algorithm. SCM is a method of clustering which allows a data point to belong to two or more clusters at a time. This method was developed by Dunn in 1973 [83] and improved by Bezdek in 1981 [84]. It is based on minimization of an objective function called, Mean square Error (MSE). SCM was frequently used in pattern recognition.

A detailed work on SCM can be found out from the paper [85], [86], [87], [88], [89], [90], [91], [91], [92], [93].

Several work has been also done on gene expression analysis using SCM [94],[95], [96], [97], [98], [99], [100], [101].

3.2.3 Review on Genetic Algorithm based Clustering

Clustering can be formally formulated as a NP-hard grouping problem in optimization perspective [102]. This research finding has stimulated the search for efficient approximation algorithms, including not only the use of ad-hoc heuristics for particular classes or instances of problems, but also the use of general-purpose metaheuristics [103]. Particularly, evolutionary algorithms are metaheuristics widely believed to be effective on NP-hard problems, being able to provide near-optimal solutions to such problems in reasonable time. Under this assumption, a large number of evolutionary algorithms for solving clustering problems have been proposed in the literature [34]. These algorithms are based on the optimization of some objective function (i.e., the so-called $fitness\ function$) that guides the evolutionary search. In evolutionary algorithm, Genetic algorithm (GA) becomes natural choice for cluster formation algorithm due to its wide applicability in wide range of areas. Problem representation is one of the key decision to be made when applying a GA to a problem. Problem representation in a GA individual determines the shape of the solution space that a GA must search. As a result, *different encodings of the same problem are essentially different problems for a GA* [104]. The application of GAs for solving problems of pattern recognition appears to be appropriate and natural. Research articles in this area have reported in literature [105], [106], [107], [108], [109], [110], [111], [112], [113], [114]. An application of GAs has been also reported in the area of (supervised) pattern classification for designing a GA-classifier [107], [115]. GA based Clustering algorithm for machine learning data was reported in the literature [116], [17], [117], [118].

The paper [17] is specific to pattern recognition data. There are no extensive work reported in literature for bioinformatics data specially for microarray cancer data using GA.

3.3 Conclusion

Due to advancement of DNA microarray technology, researchers now have the ability to collect expression data on every gene in a cell simultaneously. The vast datasets created with this technology are providing valuable information that can be used to accurately diagnose, prevent, or cure a wide range of genetic and infectious diseases. Thus, an area of active research is the development of tools to accurately collect, analyze, and interpret massive quantities of data on gene expression levels in the cell. There are several examples in the literature where computational tools have been applied to analyze gene expression data. The summary of these microarray data and tools are given in Table 3.1 ([45]).

Table 3.1: Summary of work done in Literature on Microarray using classification(supervised/unsupervised) Source: [45]

Data Set	Description	Method
Cho's Data [39]	6,200 ORFs in S cerevisiae with 15 time points	K-Means [18], SOM [19], CLICK [20], DHC [21], Biclustering [31], δ -Cluster [32]
Iyer's Data [35]	9.800 cDNAs with 12 time points	agglomerative hierarchical [23], [20], DHC [21]
Wen's Data [119]	112 rat genes during 9 time points	CAST [22]
Combined yeast Data [36], [120], [37]	6,178 ORFs in S cerevisiae with 4 time courses	agglomerative hierarchical [23], model-based [121], Plaidmodel [33]
Colon cancer data [122]	6,500 human genes in 40 tumor and 22normal colon tissue samples	divisive hierarchical [122], model-based [24]
C.elegans data	1,246 genes in 146 experiments	CAST [22]
human hematopoietic data	(1)6,000 genes in HL-60 cell lines with 4 time points (2)6,000 genes in 4 cell lines (HL-60, U937 and jurkat with 4 time points and NB4 with 5 time points)	SOM [19]
Leukemia Data [41]	7,129 genes, 72 Samples (25 AML, 47 All)	Some supervised methods Xing et. al. [25] and Ding et. al. [26], CTWC [30]
Lymphoma Data [123]	4,096 genes, 96 Samples(46 DLBCL, 50 Normal)	Some supervised methods Ding et. al. [26], Hastie et al. [27], Biclustering [31]
Colon cancer Data [122]	2,000 genes, 62 Samples	Some supervised methods, CTWC [30]
Hereditary Breast cancer Data	3,226 genes, 22 Samples(7 BRCA1,8BRCA2,7Sporadic)	Some supervised methods
Multiple Sclerosis data [124]	4,132 genes, 44 Samples (15 MS, 14 IFN, 15 Control)	Tang et al. [28], [29]

Chapter 4

Comparative Study On Hard C-means and Soft C-means Clustering Algorithm

Clustering techniques can be broadly divided into two types: Hard and Soft clustering algorithm. A Hard clustering algorithm allocates each pattern (or, data point) to a single cluster during its operation and in its output whereas a soft clustering method assigns degrees of membership in several clusters to each input pattern. A soft clustering can be converted to a hard clustering by assigning each pattern to the cluster with the largest measure of membership [10]. In this chapter, study has been carried out on Hard C-means (HCM) clustering and Soft C-means (SCM) clustering algorithm.

This chapter is broadly divided into four section:

- Experimental Setup to simulate Hard C-means and Soft C-means clustering algorithm
- Hard C-means Clustering Algorithm ([7], [8], [9], [10])
- Soft C-means Clustering Algorithm ([83], [84])
- Comparative studies on HCM Clustering Algorithm and SCM Clustering Algorithm

4.1 Experimental Setup

In this section, details about various datasets used for simulating cluster formation algorithm to solve “gene expression analysis problem” has been given. Two pattern recognition data and thirteen bioinformatics data were taken for simulation study. Study has been made on almost all benchmark bioinformatics data reported in last decade in literature. In order to identify common subtypes (cluster within clusters) in independent disease data: four different types of breast data (Golub et. al) and four DLBCL (Diffused Large B-cell Lymphoma) data are considered for our study on both gene/sample data as well as time series microarray data. The short description of the datasets along with their size, no. of clusters and source of the data has been given in Table 4.1. These datasets are having both overlapping and non-overlapping class boundaries, where the number of features/genes ranges from 4 to 7129 and number of sample ranges from 32 to 683. The number of cluster ranges from 2 to 11. Details about these data can be found out from respective referenced paper. All the data have been pre-processed in such a way that all the data point which belongs to class 1 in original datasets is kept together, then all the data points which belong to class 2 is kept together and so on. The reference vector (class information) of resultant data are given in appendix B. The snap shots of a dataset (e.g., iris data) is given in appendix A. The details of all the fifteen datasets are given in subsection below.

4.1.1 Datasets

This section deals with dataset used to simulate proposed clustering algorithm. *'Two'* machine learning and *'thirteen'* bioinformatics data have been taken to simulate clustering algorithm to solve "gene expression analysis problem". Brief introduction about the data is given below:

Machine Learning Data (Pattern Recognition Data)

1. **Iris Data**

   The Iris data set [125] is a well known and well used benchmark data set used in the machine learning community. The dataset consists of three varieties of Iris; Setosa, Virginica and Versicolor. There are '150' instances of plants that make up the three classes. The data consists of four independent variables. These variables are measurement of the flowers of the plants such as sepal and petal lengths. Since the data are labeled, it has been extensively used for classification purpose in previous work. For clustering, the labeled information available to Iris data was not used while forming clusters. The size of the data is

[150x4].The characteristic of this data is it's having some overlap between classes 2 and 3. The minimum and maximum feature values in Iris are 0.1 and 7.7. Since the number of classes in this data is three therefore the value of the 'C' chosen to be 3. The original data can be obtained from UCI repository websites: http://archive.ics.uci.edu/ml/datasets/Iris). The snap shots of iris data is given in appendix A.

2. **Wisconsin Breast Cancer Data (WBCD)**

   Breast cancer is one of the most common cancers in women and a frequent cause of death in the 35-55 year age group. The presence of a breast mass is an alert sign, but it does not always indicate a malignant cancer. Non-invasive diagnostic test (e.g., Fine needle aspiration of breast masses), that obtains information needed to evaluate malignancy. The Wisconsin Breast Cancer dataset was initially created to conduct experiments that were to prove the usefulness of automation of fine needle aspiration cytological diagnosis. It contains 699 instances of cytological analysis of fine needle aspiration from breast tumors. Each case comprises 11 attributes: a case ID, cytology data (normalized, with values in the range '1-10') and a benign/malignant attribute. The number of benign instances is '458' (65.52%) and the number of malignant instances is '241' (34.48%). Sixteen instances of cases ('14' benign, '2' malignant) with missing values has been removed from the dataset for simulation study. The original WBCD data [126], [127] can be downloaded from UCI repository websites (http://archive.ics.uci.edu).

   Gene Expression Microarray Data (Bioinformatics Data)

   The gene expression datasets and a very short description of their characteristics are given in Table 4.1. Further biological details about these data sets can be found in the referenced papers. Most data were processed on the Human Genome U95 Affymetrix "*c*" microarrays. The Leukemia dataset is from the previous-generation Human Genome HU6800 Affymetrix '*c*' microarray.

3. **Iyer data (serum data)**

   This data set is previously described and has been used in paper [35]. It can be downloaded from: http: //www.sciencemag.org/feature/data/984559.shl. It corresponds to the selection of '517' genes whose expression varies in response to serum concentration in human fibroblasts and is classified into '11' groups.

4. **Cho data (Yeast data)**

   In this data set [39], [18] the expression pro-files of 6200 yeast genes were measured every 10 minute during two cell cycles in 17 hybridization experiments. Tavazoie et. al. [18] used the Yeast data of 2945 genes. He selected the data after excluding time points 90 and 100 minute from Yeast data. In this thesis, 386 genes from Cho data has been considered for analysis of experimental work [128]. Total no. of classes for this data is 5.

5. **Leukemia (Golub experiment)**

   The Leukemia dataset belongs to two types of Leukemia cancers [41], [129]: Acute Myeloid Leukemia (AML) and Acute Lymphoblastic Leukemia (ALL). It consists of '72' samples of '7129' gene expressions each. The data has '47' samples belong to ALL cancer class and '25' samples belong to AML cancer class.

Breast data

The microarray breast data used in this paper can be downloaded from http://www.broad.mit.edu/cgi-bin/cancer/datasets.cgi.

6. **Breast data A** [42]

   This data is of dimension [98x1213] and total number of classes for this data is three.

7. **Breast data B** [43]

   This data is of dimension [49x1024] and total number of classes for this data is three.

8. **Breast Multi data A** [130]

   This data is of dimension [103x5565] and total number of classes for this data is four.

9. **Breast Multi data B** [131]

   This data is of dimension [32x5565] and total number of classes for this data is four.

   Lymphoma data (Alizadeh et al. Experiment)

   This datsets describes systematic characterization of gene expression patterns in the most prevalent adult Lymphoid malignancies: Diffused Large B Cell Lymphoma (DLBCL) [123]. In addition, non-lymphoma (normal) samples are also involved because of the suspected correlation between them and the three malignances. Within DLBCL class, there are two molecularly distinct forms of DLBCL which have gene expression patterns indicative of different stages of B-cell differentiation (1. Germinal centre B cells ('GC B-like DLBCL'); 2.'Activated B-like DLBCL'). These two subtypes of DLBCL have clinically distinct meanings: patients with germinal centre B-like DLBCL have a significantly better overall survival than those with activated B-like DLBCL. The molecular classification of tumors on the basis of gene expression can thus identify previously undetected and clinically significant subtypes of cancer. Four subtypes of DLBCL (DLBCL A, DLBCL B, DLBCL C, DLBCL D) has been used to analyze experimental work. All these Data can be downloaded from http://www.broad.mit.edu/cgi-bin/cancer/datasets.cgi.

10. **DLBCL A** [132]

    The size of DLBCL A data is [141 X 661] and number of cluster is three.

11. **DLBCL B** [133]

    The size of DLBCL B data is [180 X 661] and number of cluster is three.

12. **DLBCL C** [44]

    The size of DLBCL C data is [58 X 1772] and number of cluster is four.

13. **DLBCL D** [132]

    The size of DLBCL D data is [129 X 3795] and number of cluster is four.

14. **Lung Cancer** [40]

    This microarray datasets [40] is of dimension [197x581]. It includes 4 known classes: 139 adenocarcinomas (AD), 21 squamous cell carcinomas (SQ), 20 carcinoids (COID), and 17 normal lung (NL). The AD class is highly heterogeneous, and substructure is known to exist, although not well understood. The source of data is: http://www.broad.mit.edu/cgi-bin/cancer/datasets.cgi .

15. **St. Jude Leukemia data** [134]

    This datasets [134] is of diagnostic bone marrow samples from pediatric acute Leukemia patients corresponding to 6 prognostically important Leukemia subtypes: 43 T-lineage ALL; 27 E2A-PBX1, 15 BCR-ABL, 79 TEL-AML1, and 20 MLL rearrangements; and 64 ”hyperdiploid $\geq$ 50” chromosomes. The source of data is: http://www.broad.mit.edu/cgi-bin/cancer/datasets.cgi .

Table 4.1: Datasets with known ground truth value (i.e. class label information are known)

Sl. No.	**Datasets**	**Source**	**Dimension**	**Number of cluster**
1	Iris	[125]	[150x4]	3
2	WBCD	[126], [127]	[683x9]	2
3	Iyer data/Serum data	[35]	[517x12]	11
4	Cho data (yeast data)	[39] [18]	[386x16]	5
5	Leukemia (Golub xperiment)	[41], [129]	[72x7129]	2
6	Breast data A	[42]	[98x1213]	3
7	Breast data B	[43]	[49x1024]	4
8	Breast Multi data A	[130]	[103x5565]	4
9	Breast Multi data B	[131]	[32x5565]	4
10	DLBCL A	[132]	[141x661]	3
11	DLBCL B	[133]	[180x661]	3
12	DLBCL C	[44]	[58x1772]	4
13	DLBCL D	[132]	[129x3795]	4
14	Lung Cancer	[40]	[197x581]	4
15	St. Jude Leukemia data	[134]	[248x985]	6

In next section (section 4.2), First discussion has been made on basic steps involved in HCM Clustering Algorithm and then how it can be used for Gene/Sample clustering.

4.2 Hard C-means (HCM) Clustering Algorithm

This section describes HCM clustering algorithm and their application to machine intelligence data as well as to bioinformatics data. First, basic steps involved in HCM

Table 4.2: Hard C-means Clustering Algorithm

Notations: X: Datasets; X_i: i^{th} Data point of X; x: any data point in X; n : Total Number of data point in X; N : Dimension of each data; V_j= j^{th} Cluster; C : Number of Cluster v_j = j^{th} Cluster Center; v_j^* = j^{th} Cluster Center after updation; i, j, and p : index variable
Input: Given datasets X; total number of data is 'n'; each data is of dimension 'N'. Therefore dataset $X = \{X_1, X_2, \ldots, X_n\}$. Total Number of Cluster is: C.
Output: V_1, V_2,...V_C.
Objective Function: $J = \sum_{j=1}^{C} \sum_{x_i \in V_j} \lVert x_i - v_j \rVert^2$ $\quad j \in 1,2,\ldots,C$ and $i = \{1,2,\ldots,n\}$.
Hard C-means Clustering Algorithm: Step 1: Chose "C" initial cluster centers(i.e. Prototype vector) $v_1, v_2, \ldots v_C$ either randomly or using any intelligent techniques from the given 'n' data points $X_1, X_2, \ldots, X_n$. Step 2: Now compute $\lVert X_i - v_j \rVert \; and \; \lVert X_i - v_p \rVert \qquad for \;\; p \in 1,2,\ldots C, \;\; but \;\; p \neq j.$ if $\lVert X_i - v_j \rVert < \lVert X_i - v_p \rVert \qquad for \;\; p \in 1,2,\ldots C, \;\; but \;\; p \neq j$ where $X_i, i = 1,2,,n$; Then put data X in cluster V_j. If any ties occurred, then resolved it arbitrarily. Step 3: Compute new cluster centers $\{v_1^*, v_2^*, ..., v_c^*\}$ as follows: $v_j^* = \frac{1}{\lvert V_j \rvert} \sum_{x_i \in V_j} x_i$, $\qquad j = 1,2,\ldots,C,$ Where $\lvert V_j \rvert$ = is the number of elements belonging to cluster V_j. Step 4: If $v_j^* = v_j$; $j = 1,2,\ldots,C$; then terminate. Otherwise repeat from step 2. Step 5: If the process does not terminate at Step 4 normally, then it is executed for a maximum "fixed number of iterations".

clustering algorithm has been explained in details and then experiment are carried out to assess the performance of HCM clustering algorithm.

The HCM clustering algorithm ([7], [8], [9], [10]), one of the most widely used clustering techniques, attempts to solve the clustering problem by optimizing a objective function J, which is Mean Square Error (MSE) of formed cluster. The objective function J is given as follows: $Minimize(J) = \sum_{j=1}^{C} \sum_{x_i \in V_j} \| x_i - v_j \|^2 \qquad j \in 1,2,\ldots,C$ and $i = \{1,2,\ldots,n\}$.

The basic steps involved in HCM clustering algorithm are briefly described in Table 4.2.

4.2.1 Result And Discussions

To validate the feasibility and performance of the HCM clustering algorithm, HCM clustering has been implemented in MATLAB 7.0 (Intel C2D processor, 2.0 GHz, 2 GB RAM) and applied it to Machine learning data as well as to bioinformatics data. Since the datasets used for simulation studies possess class label information, *clustering accuracy* has been used as cluster validation metric to judge quality of the cluster formation algorithm. *Clustering Accuracy* is defined as follows:

$$Clustering\ Accuracy \ = (\frac{Number\ of\ Correct\ Count}{Total\ number\ of\ instances\ genes/samples}) * 100$$

. Complete result of Hard C-means clustering for machine learning and bioinformatics data has been given in appendix C and appendix E. Appendix C contains the details of data distribution after simulation of HCM clustering algorithm and Appendix E contains the details of data point wrongly clustered in each cluster after simulation of HCM clustering algorithm. Here in this section, result obtained for HCM clustering algorithm has been discussed in brief.

Table 4.3 represents summary of result using HCM clustering algorithm for fifteen datasets. It also consists of some important relevant characteristics, such as number of classes, number of features/genes and the number of item samples. Out of fifteen datasets maximum accuracy was reported for WBCD data while least accuracy data was reported for DLBCL D (Table 4.3). As far as gene expression data is concerned maximum accuracy was achieved in case of St. Jude Leukemia data (Table 4.3).

Table 4.4 represents the result of Iris data. Overall accuracy has been achieved upto 88.67%. The total count error in this case is 17. It may be noted that 100% accuracy has been obtained for cluster 1. Similar sort of result for Iris data has been also reported in literature [47], [48], [49].

Table 4.6 represents the result of Serum data (Iyer data). Accuracy upto 51.84% has been obtained in this case.

Table 4.5 represents the result of WBCD data. 95.75% accuracy has been achieved in this case.

Table 4.7 represents the result of Yeast data (Cho data). Overall Accuracy upto 60.88 % has been obtained for this data. It may be noted that cluster 4 is having lowest accuracy of 12%. The reason for this is that data belonging to this cluster are very much overlapping in nature with other clusters.

Table 4.8 represents the result of Leukemia data. Over all accuracy upto 59.72% has been obtained. The Golub et. al.'s microarray data [41], [129] is very challenging because the appearance of the two types of acute Lseukemia features are highly similar in nature. This was the reason, accuracy was low in this case. One probable solution of this problem could be the use of *dimensionality reduction* techniques to reduce the number of features and then use HCM clustering algorithm.

Table 4.9 to Table 4.12 represents the result of subtypes of Breast data. Maximum accuracy was obtained for Breast Multi data A (79.61%) whereas the least accuracy for Breast data B was (53.06%). The reason of the less accuracy could be probably Breast data B is more overlapping in nature and is having nonlinear structure.

Table 4.13 to Table 4.16 represents the result of subtypes of DLBCL data (Diffused Large B-cell Lymphoma). DLBCL D is of highly overlapping in nature and that's why least accuracy of 42.64% has been obtained in this case. The data of DLBCL B is of highly distinctively separated in nature compared to other data such as DLBCL (A, C, D) and that is the reason higher accuracy was obtained in case of DLBCL B.

Table 4.17 represents the result of Lung Cancer. Accuracy upto 72.08% has been obtained. In this, cluster 2 and cluster 4 are highly separable in nature compared to cluster 1 and cluster 3. 95% accuracy was obtained for cluster 2 and cluster 4, whereas least accuracy was obtained for cluster 3 i.e., 47%.

Table 4.18 represents the result of St. Jude Leukemia data. For this data accuracy upto 85.08% was obtained. The data in this case is of highly separable in nature. 100% accuracy has been obtained for cluster 2 and least one was obtained for cluster 5.

Table 4.3: Summary of Results for Hard C-means using all fifteen datasets

Sl. No.	Datasets	Dimension	# of cluster	Hard C-means			
				# Error	Error (%)	# correct	Accuracy (%)
1	Iris	[150x4]	3	17	11.33	133	88.67
2	WBCD	[683x9]	2	29	4.25	654	95.75
3	Iyer data/Serum data	[517x12]	11	249	48.1624	268	51.84
4	Cho data (yeast data)	[386x16]	5	151	39.1191	235	60.88
5	Leukemia(Golub Experiment)	[72x7129]	2	29	40.28	43	59.72
6	Breast data A	[98x1213]	3	27	27.55	71	72.44
7	Breast data B	[49x1024]	4	23	46.93	26	53.0612
8	Breast Multi data A	[103x5565]	4	21	20.39	82	79.61
9	Breast Multi data B	[32x5565]	4	15	48.88	17	53.125
10	DLBCL A	[141x661]	3	66	46.8085	75	53.191
11	DLBCL B	[180x661]	3	40	22.22	140	77.78
12	DLBCL C	[58x1772]	4	28	48.28	30	51.7241
13	DLBCL D	[129x3795]	4	74	57.36	55	42.64
14	Lung Cancer	[197x581]	4	55	27.92	142	72.0812
15	St. Jude Leukemia data	[248x985]	6	37	14.91	211	85.08

Table 4.4: Result of Iris Data (Hard C-means)

	Cluster 1	Cluster 2	Cluster 3	Total
The right number of data point	50	50	50	150
The number of data point wrongly clustered	0	4	13	17
The number of data point correctly clustered	50	46	37	133
Accuracy (%)	100	92	74	88.67

Table 4.5: Result of WBCD Data (Hard C-means)

	Cluster 1	Cluster 2	Total
The right number of data point	444	239	683
The number of data point wrongly clustered	9	20	29
The number of data point correctly clustered	435	219	654
Accuracy (%)	97.97	91.63	95.75

Table 4.6: Result of Serum data (Hard C-means)

	Cluster1	Cluster2	Cluster3	Cluster4	Cluster5	Cluster6	Cluster7	Cluster8	Cluster9	Cluster10	Cluster11	Total
The right number of data point	33	100	145	34	43	7	34	14	63	19	25	517
number of data point wrongly clustered	17	84	7	34	31	6	17	1	28	12	12	249
number of data point correctly clustered	16	16	138	0	12	1	17	13	35	7	13	268
Accuracy	48.48	16	95.17	0	27.91	14.29	50	92.86	55.56	36.84	52	51.84

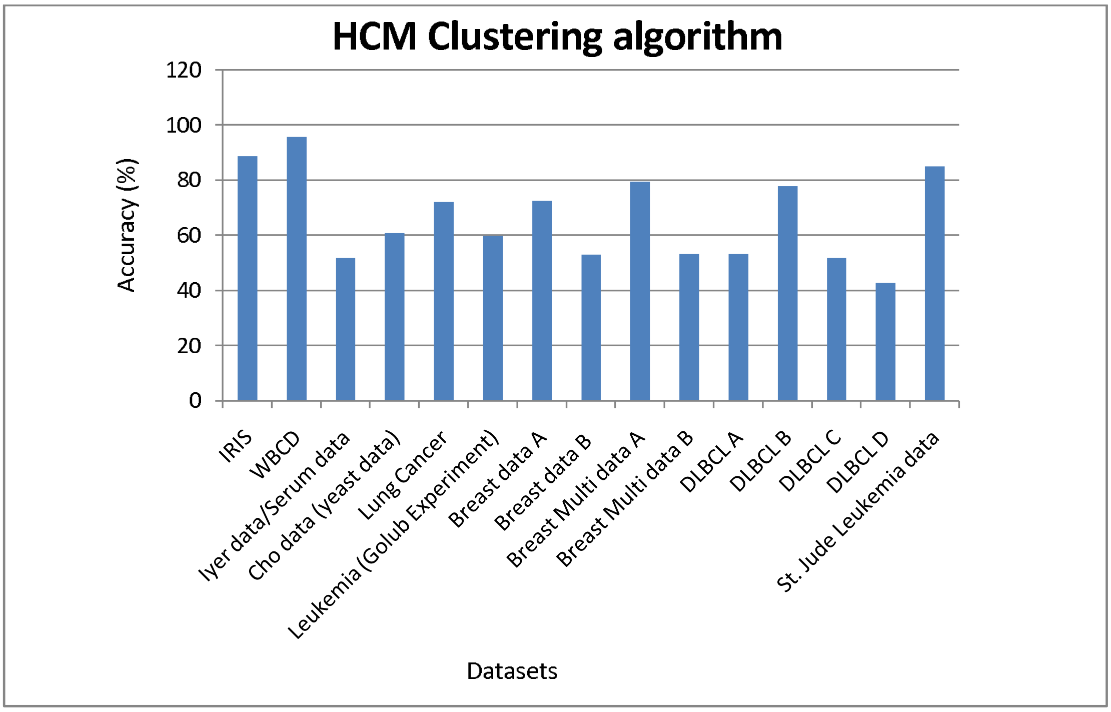


Figure 4.1: Clustering accuracy of HCM using all fifteen data.

Table 4.7: Result of Cho Data (Hard C-means)

	Cluster 1	Cluster 2	Cluster 3	Cluster 4	Cluster 5	Total
The right number of data point	67	135	75	54	55	386
The number of data point wrongly clustered	30	25	28	47	21	151
The number of data point correctly clustered	37	110	47	7	34	235
Accuracy %	55.22	81.48	62.67	12.96	61.82	60.88

Table 4.8: Result of Leukemia Data/Golub Experiment (Hard C-means)

	Cluster 1	Cluster 2	Total
The right number of data point	47	25	72
The number of data point wrongly clustered	15	14	29
The number of data point correctly clustered	32	11	43
Accuracy (%)	68.09	44	59.72

Table 4.9: Result of Breast data A (Hard C-means)

	Cluster 1	Cluster 2	Cluster 3	Total
The right number of data point	11	51	36	98
number of data point wrongly clustered	1	22	4	27
number of data point correctly clustered	10	29	32	71
Accuracy(%)	90.91	56.86	88.89	72.44

Table 4.10: Result of Breast data B (Hard C-means)

	Cluster 1	Cluster 2	Cluster 3	Cluster 4	Total
The right number of data point	12	11	7	19	49
Number of data point wrongly clustered	0	5	5	13	23
Number of data point correctly clustered	12	6	2	6	26
Accuracy(%)	100	54.54	28.57	31.58	53.06

Table 4.11: Result of Breast Multi data A (Hard C-means)

	Cluster 1	Cluster 2	Cluster 3	Cluster 4	Total
The right number of data point	26	26	28	23	103
The number of data point wrongly clustered	2	1	18	0	21
The number of data point correctly clustered	24	25	10	23	82
Accuracy (%)	92.31	96.15	35.71	100	79.61

Table 4.12: Result of Breast Multi data B (Hard C-means)

	Cluster 1	Cluster 2	Cluster 3	Cluster 4	Total
The right number of data point	5	9	7	11	32
The number of data point wrongly clustered	3	2	3	7	15
The number of data point correctly clustered	2	7	4	4	17
Accuracy (%)	40	77.78	57.14	36.36	53.13

Table 4.13: Result of DLBCL A (Hard C-means)

	Cluster 1	Cluster 2	Cluster 3	Total
The right number of data point	49	50	42	141
The number of data point wrongly clustered	26	22	18	66
The number of data point correctly clustered	23	28	24	75
Accuracy (%)	46.94	56	57.14	53.19

Table 4.14: Result of DLBCL B (Hard C-means)

	Cluster 1	Cluster 2	Cluster 3	Total
The right number of data point	42	51	87	180
The number of data point wrongly clustered	18	7	15	40
The number of data point correctly clustered	24	44	72	140
Accuracy (%)	57.14	86.27	82.76	77.78

Table 4.15: Result of DLBCL C (Hard C-means)

	Cluster 1	Cluster 2	Cluster 3	Cluster 4	Total
The right number of data point	17	16	13	12	58
The number of data point wrongly clustered	1	9	12	6	28
The number of data point correctly clustered	16	7	1	6	30
Accuracy (%)	94.11	43.75	7.69	50	51.72

Table 4.16: Result of DLBCL D (Hard C-means)

	Cluster 1	Cluster 2	Cluster 3	Cluster 4	Total
The right number of data point	19	37	24	49	129
The number of data point wrongly clustered	13	28	13	20	74
The number of data point correctly clustered	6	9	11	29	55
Accuracy (%)	31.58	24.32	45.83	59.18	42.64

Table 4.17: Result of Lung Cancer (Hard C-means)

	Cluster 1	Cluster 2	Cluster 3	Cluster 4	Total
The right number of data point	139	17	21	20	197
The number of data point wrongly clustered	42	1	11	1	55
The number of data point correctly clustered	97	16	10	19	142
Accuracy (%)	69.78	94.11	47.62	95	72.08

Table 4.18: Result of St. Jude Leukemia data (Hard C-means)

	Cluster1	Cluster2	Cluster3	Cluster4	Cluster5	Cluster6	Total
The right number of data point	15	27	64	20	43	79	248
The number of data point wrongly clustered	15	0	3	4	14	1	37
The number of data point correctly clustered	0	27	61	16	29	78	211
Accuracy (%)	0	100	95.31	80	67.44	98.73	85.08

In next section (section 4.3), First discussion has been made on basic steps involved in Soft C-means Algorithm and then how it can be used for Gene/Sample clustering.

4.3 Soft C-means (SCM) Clustering Algorithm

The Soft C-means Algorithm (SCM), which is also known as Fuzzy C-Means algorithm (FCM) [83], [84], [135], generalizes the Hard C-means algorithm, to allow data points to partially belonging to multiple clusters at same time. Therefore, it produces a soft partition for a given data set. In fact, it generates a constrained soft partition. To achieve this, the objective function of HCM clustering algorithm has to be extended in two ways:

1. Incorporation of degree of fuzzy membership in clusters $\{V_1, V_2, \ldots, V_C\}$ and
2. An introduction of fuzziness parameter 'm', a weight exponent in the fuzzy membership.

The extended objective function J (MSE, Mean square error) is defined as follows:

$$Minimize\ (J) \ = \ \sum_{j=1}^{C} \sum_{x_i \in V_j} (\mu V_j(x_i))^m \| \ x_i - v_j \ \|^2 \quad for \quad j \in 1,2,\ldots,C \text{ and } i = \{1,2,\ldots,n\}.$$

Where V is a fuzzy partition of the data set X formed by clusters $\{V_1, V_2, \ldots, V_C\}$. The parameter '$m$' is a weight that determines the degree to which partial members of a cluster affect the clustering result.

Like HCM clustering algorithm, the SCM clustering algorithm tries to find a good partition by searching prototypes (i.e., cluster center) v_j that minimize the objective function 'J'. Unlike HCM, however, the SCM algorithm also needs to search for membership functions μV_j that minimizes 'J' . To accomplish these two objective, SCM Theorem has been proposed by Bezdek in 1981 ([84], [135]), which is given below:

Theorem 1: Soft C-Means Theorem A constrained soft partition $\{V_1, V_2, \ldots, V_C\}$ is a local minimum of the objective function 'J' only if the following conditions are satisfied:

$$\mu V_j(x) = \frac{1}{\left[\sum_{i=1}^{i=C} \left(\| \ x - v_j \ \|^2 / \| \ x - v_i \ \|^2 \right)^{(1/m-1)} \right]} \quad \text{for } 1 \leq i \leq C, \ \ x \ \in \ X$$

$$v_j = \frac{[\sum_x \mu V_j(x)^{(m)}(x)]}{[\ \ \sum_x \mu V_j(x)^{(m)}]} \qquad for\ 1 \leq j \leq C\ .$$

The SCM clustering algorithm can be specified as follows:

Table 4.19: Soft C-means clustering algorithm

Notations:
X: Datasets ;

X_i: i^{th} Data point

n : Total Number of Data point

N : Dimension of each data
C : Number of Cluster;

V_j= j^{th} Cluster

v_j= j^{th} Cluster center

v_j^*= j^{th} Cluster center after updation

m : Fuzziness parameter (i.e. weighted exponent of the objective function).

$\mu V_j(x)$: membership of data point x in Cluster V_j.

U_{ij} : membership of data point i in cluster j.

ε: Threshold value (usually very small) for the convergence criteria.
$i,\ j,\ and\ p$: index variable

Input:

1. given datasets X; total number of data is n; each data is of dimension 'N'. Therefore dataset $X = \{X_1, X_2, \ldots, X_n\}$.
Toatl Number of Cluster is: C.

Output:

$V_{1,}V_2, \ldots, V_C$.

Objective Function: Mean Square Error:

$Minimize\ (J)\ =\ \sum_{j=1}^{C} \sum_{x_i \in V_j} (\mu V_j(x_i))^m \| x_i - v_j \|^2 \quad for\ \ j \in 1,2,\ldots,C$ and $i = \{1,2,\ldots,n\}$.

SCM clustering Algorithm:

```
Step 1: Select "$C$" initial cluster centers randomly $V = \{v_1, v_2, ..., v_c\}$ and membership matix U.
Step 2: Make $U(old) \leftarrow U$.
Step 3: Calculate membership functions as follows:
$\mu V_j(x) = \frac{1}{\left[\sum_i \left(\|x-v_j\|^2/\|x-v_i\|^2\right)^{(1/m-1)}\right]} \quad for\ 1 \le j \le C,\ x \in\ X$
Step 4: Update the cluster $v_j$ in $V$.
$v_j^* = \frac{[\sum_x \mu V_j(x)^{(m)}(x)]}{[\ \sum_x \mu V_j(x)^{(m)}]} \quad for\ 1 \le j \le C.$
Step 5: Calculate $E = \sum \| U_{old} - U \|$
Step 6: If $E > \varepsilon$ ; then go to Step 2.
Step 7: If $E \le \varepsilon$; then output the final result.
```

In the previous algorithm, 'C' is the number of clusters to form, 'm' is the parameter of the objective function, and ε is a threshold value (usually very small) for the convergence criteria. The SCM algorithm is guaranteed to converge for $m > 1$. This important convergence theorem was established by Bezdek in 1981 [84], [135] . SCM finds a local minimum of the objective function 'J'. This is because the SCM theorem is derived from the condition that the gradient of 'J' should be zero for a SCM solution, which is satisfied by all the local minimums. Finally, it can be concluded that the result of applying SCM to a given data set depends not only on the choice of the parameters 'm' and 'C', but also on the choice of the initial prototypes i.e., initial cluster distribution.

4.3.1 Discussion on parameter selection in SCM

The proper selection of fuzziness parameter 'm' is an important and tough task in SCM clustering algorithm, which directly affects the performance of algorithm and the validity of soft cluster analysis. Lots of work on study of the soft exponent 'm' has been reported in literature. The value of 'm' should be always greater than 1 for SCM to be converging for optimal solution [84], [135]. In the literature about SCM, m is commonly fixed to 2 [136]. '2' is not an appropriate fuzziness parameter for microarray data [95]. For '$m = 2$', for the microarray datasets, it was found that in many of the cases, SCM failed to extract any clustering structure underlying within data, since all the membership values became similar. It was shown in paper [95] that when 'm' goes to infinity, values of U_{ij} tends to $1/C$. Thus, for a given data set, there is an upper bound value for 'm', above which the membership values resulting from SCM are equal to $1/C$. When higher 'm' values are used, the U_{ij} distribution becomes more spread out. With a lower value of 'm' all genes become strongly associated to only one cluster, and the clustering is similar to that obtained with HCM. Thus, the selected value for 'm' appears to be a good compromise between the need to assign most genes to a given cluster, and the need to discriminate genes that classify poorly [95].

4.3.2 Result and Discussions

Parameter used in SCM is given in Table 4.20.

Complete result of Soft C-means clustering for machine learning and bioinformatics data has been given in appendix D and appendix E. Appendix D contains the details of data distribution after simulation of SCM clustering algorithm and Appendix E contains the details of data point wrongly clustered in each cluster after simulation of SCM clustering algorithm. Here in this section, result obtained for SCM clustering algorithm has been stated in brief.

Table 4.21 represents summary of result of SCM clustering algorithm result for fifteen datasets (fig. 4.2). It consists some of the relevant characteristics, such as number of classes, number of features/genes and the number of item samples. These datasets are having both overlapping and non-overlapping class boundaries, where the number of features/genes ranges from 4 to 7129 and number of sample ranges from 32 to 683. The number of cluster ranges from 2 to 11.

Table 4.22 represents the result of Iris data. Overall accuracy was achieved upto 90.67 %. The total count error in this case is 14. It may be noted that 100 % of accuracy was achieved for cluster 1.

Table 4.23 represents the result of WBCD data. 96.05% accuracy was achieved in this case.

Table 4.24 represents the result of Serum data (Iyer data). Overall accuracy was achieved upto 48.74%.

Table 4.25 represents the result of Yeast data (Cho data). Overall accuracy was achieved upto 63.73%. Note that cluster 3 is having accuracy approx. 36%. The reason for this is the data belonging to this cluster are very overlapping in nature with other clusters.

Table 4.26 represents the result of Leukemia data. Overall accuracy was achieved upto 55.56%. The Golub et. al.'s microarray data set is very challenging because the appearance of the two types of acute Leukemia features are highly similar in nature. This was the reason less accuracy was achieved in this case. One probable solution this problem could be use of dimensionality reduction techniques to reduce the number of features.

Table 4.27 to Table 4.30 represents the result of subtypes of Breast data. Maximum accuracy was achieved for Breast multi data A (90.29%) whereas the least accuracy was achieved for Breast multi data B (50%). The reason of this could be probably Breast data B is more overlapping in nature and is having nonlinear structure.

Table 4.31 to Table 4.34 represents the result of subtypes of DLBCL data (Diffused Large B-cell Lymphoma). DLBCL D is of highly overlapping nature and that's why least accuracy 50.38% was achieved in this case. The data of DLBCL C is of highly distinctively separated in nature compared to other DLBCL (A, B, D) and that is the reason higher accuracy was achieved in case of DLBCL C.

Table 4.35 represents the result of Lung Cancer. Overall accuracy was achieved upto 76.14%. In this, cluster 2 and cluster 4 are highly separable in nature compared to cluster 1 and cluster 3. Highest accuracy was achieved for cluster 4 (95 %) and least accuracy for cluster 3 (61%).

Table 4.36 represents the result of St. Jude Leukemia data. Overall accuracy was achieved upto 88.31%. The data in this case is of highly separable in nature. It may be noted that 100% accuracy was achieved for cluster 6 and least one was for cluster 1.

Fig. 4.3 to fig. 4.17 shows convergence graph of Soft C-means clustering algorithm for all fifteen datasets. Here the X-axis represents number of iteration carried out while Y-axis represents threshold value E.

Table 4.20: Parameters used in SCM

Sl. No.	Datasets	mfuz (m)	Maximum Iteration no. taken for convergence
1	Iris	4.2	1000
2	WBCD	1.58	20
3	Iyer data/Serum data	1.92	336
4	Cho data (yeast data)	2.15	241
5	Leukemia (Golub Experiment)	1.28	1000
6	Breast data A	1.6	311
7	Breast data B	1.15	194
8	Breast Multi data A	1.3	71
9	Breast Multi data B	1.795	576
10	DLBCL A	1.40	138
11	DLBCL B	1.285	419
12	DLBCL C	1.345	114
13	DLBCL D	1.25	423
14	Lung Cancer	1.07	65
15	St. Jude Leukemia data	1.26	165

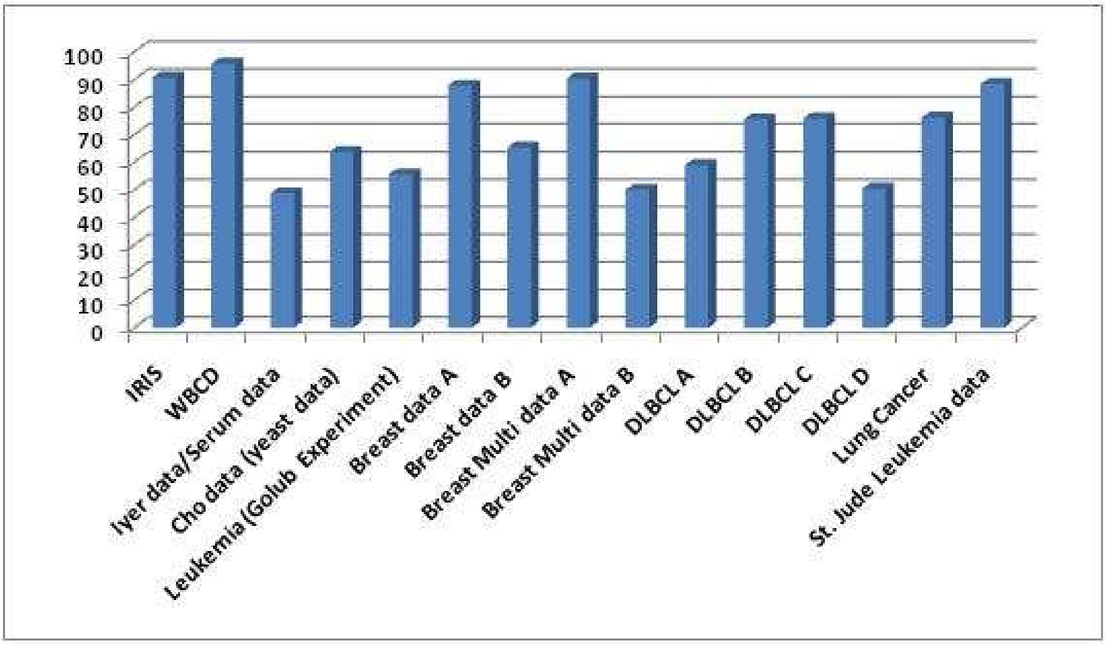


Figure 4.2: Clustering accuracy of SCM for pattern recognition as well as microarray data.

Table 4.21: Summary of Results for Soft C-means using all fifteen datasets

Datasets	**Dimen sion**	**# cluster**	**SCM**					
			mfuz (m)	Iterat ion no .	# Error	Error (%)	# correct	Accur acy(%)
Iris	[150x4]	3	4.2	1000	14	9.33	136	90.67
WBCD	[683x9]	2	1.58	20	29	3.95	656	96.05
Iyer data/Serum data	[517x12]	11	1.92	336	265	51.26	252	48.74
Cho data (yeast data)	[386x16]	5	2.15	241	140	36.27	246	63.73
Leukemia (Golub Experiment)	[72x7129]	2	1.28	1000	32	44.44	40	55.56
Breast data A	[98x1213]	3	1.6	311	12	12.25	86	87.75
Breast data B	[49x1024]	4	1.15	194	17	34.7	32	65.30
Breast Multi data A	[103x5565]	4	1.3	71	10	9.71	93	90.29
Breast Multi data B	[32x5565]	4	1.795	576	16	50	16	50
DLBCL A	[141x661]	3	1.40	138	58	41.14	83	58.86
DLBCL B	[180x661]	3	1.285	419	44	24.44	136	75.56
DLBCL C	[58x1772]	4	1.345	114	14	24.14	44	75.86
DLBCL D	[129x3795]	4	1.25	423	64	49.62	65	50.38
Lung Cancer	[197x581]	4	1.07	65	47	23.86	150	76.14
St. Jude Leukemia data	[248x985]	6	1.26	165	29	11.69	219	88.31

Table 4.22: Result of Iris Data (Soft C-means)

mfuz= 4.2; it=1000				
	Cluster 1	Cluster 2	Cluster 3	Total
The right number of data point	50	50	50	150
number of data point wrongly clustered	0	3	11	14
number of data point correctly clustered	50	47	39	136
Accuracy(%)	100	94	88	90.67

Table 4.23: Result of WBCD Data (Soft C-means)

mfuz= 1.58; it=20			
	Cluster 1	Cluster 2	Total
The right number of data point	444	239	683
number of data point wrongly clustered	09	20	29
number of data point correctly clustered	435	219	654
Accuracy(%)	97.97	91.63	95.75

Table 4.24: Result of Serum data /Iyer data (Soft C-means)

mfuz= 1.92; it=336												
	Cluster1	Cluster2	Cluster3	Cluster4	Cluster5	Cluster6	Cluster7	Cluster8	Cluster9	Cluster10	Cluster11	Total
The right number of data point	33	100	145	34	43	7	34	14	63	19	25	517
number of data point wrongly clustered	28	6	69	33	24	7	17	14	41	17	17	265
number of data point correctly clustered	5	94	84	1	19	0	17	0	22	2	8	252
Accur acy (%)	15.15	94	57.93	2.94	44.19	0	50	0	34.92	10.53	32	48.74

Table 4.25: Result of Cho Data (Soft C-means)

mfuz= 2.15; it=241						
	Cluster 1	Cluster 2	Cluster 3	Cluster 4	Cluster 5	Total
The right number of data point	67	135	75	54	55	386
number of data point wrongly clustered	15	55	48	15	8	141
number of data point correctly clustered	52	80	27	39	47	245
Accuracy (%)	77.62	59.3	36	72.22	85.45	63.47

Table 4.26: Result of Leukemia Data/Golub Experiment (Soft C-means)

mfuz= 1.28; it=1000			
	Cluster 1	Cluster 2	Total
The right number of data point	47	25	72
Number of data point wrongly clustered	18	14	32
Number of data point correctly clustered	29	11	40
Accuracy(%)	61.702	44	55.56

Table 4.27: Result of Breast data A (Soft C-means)

mfuz= 1.6; it=311				
	Cluster 1	Cluster 2	Cluster 3	Total
The right number of data point	11	51	36	98
number of data point wrongly clustered	11	0	1	12
number of data point correctly clustered	0	51	35	86
Accuracy(%)	0	100	97.22	87.76

Table 4.28: Result of Breast data B (Soft C-means)

mfuz= 1.15; it=1.15					
	Cluster 1	Cluster 2	Cluster 3	Cluster 4	Total
The right number of data point	12	11	7	19	49
number of data point wrongly clustered	0	5	0	12	17
number of data point correctly clustered	12	6	7	7	32
Accuracy (%)	100	54.54	100	36.84	65.31

Table 4.29: Result of Breast Multi data A (Soft C-means)

mfuz= 1.3; it=71					
	Cluster 1	Cluster 2	Cluster 3	Cluster 4	Total
The right number of data point	26	26	28	23	103
number of data point wrongly clustered	5	1	2	2	10
number of data point correctly clustered	21	25	26	21	93
Accuracy (%)	80.77	96.15	92.85	91.3	90.291

Table 4.30: Result of Breast Multi data B (Soft C-means)

mfuz= 1.795; it=576					
	Cluster 1	Cluster 2	Cluster 3	Cluster 4	Total
The right number of data point	5	9	7	11	32
number of data point wrongly clustered	3	3	4	6	16
number of data point correctly clustered	2	6	3	5	16
Accuracy (%)	40	66.67	42.86	45.45	50

Table 4.31: Result of DLBCL A (Soft C-means)

mfuz= 1.405; it=138				
	Cluster 1	Cluster 2	Cluster 3	Total
The right number of data point	49	50	42	141
number of data point wrongly clustered	18	23	17	58
number of data point correctly clustered	31	27	25	83
Accuracy (%)	63.27	54	59.52	58.87

Table 4.32: Result of DLBCL B (Soft C-means)

mfuz= 1.285; it=419				
	Cluster 1	Cluster 2	Cluster 3	Total
The right number of data point	42	51	87	180
number of data point wrongly clustered	13	16	15	44
number of data point correctly clustered	29	35	72	136
Accuracy (%)	69.05	68.63	89.66	75.56

Table 4.33: Result of DLBCL C (Soft C-means)

mfuz= 1.345; it=116					
	Cluster 1	Cluster 2	Cluster 3	Cluster 4	Total
The right number of data point	17	16	13	12	58
number of data point wrongly clustered	4	6	7	9	26
number of data point correctly clustered	13	10	6	3	32
Accuracy(%)	76.47	62.5	46.15	25	55.17

Table 4.34: Result of DLBCL D (Soft C-means)

mfuz= 1.33; it=423					
	Cluster 1	Cluster 2	Cluster 3	Cluster 4	Total
The right number of data point	19	37	24	49	129
number of data point wrongly clustered	8	19	10	27	64
number of data point correctly clustered	11	18	14	22	65
Accuracy (%)	57.9	48.65	58.33	44.89	50.39

Table 4.35: Result of Lung Cancer (Soft C-means)

mfuz= 1.07; it=65					
	Cluster 1	Cluster 2	Cluster 3	Cluster 4	Total
The right number of data point	139	17	21	20	197
number of data point wrongly clustered	36	2	8	1	47
number of data point correctly clustered	103	15	13	19	150
Accuracy (%)	74.1	88.24	61.9	95	76.14

Table 4.36: Result of St. Jude Leukemia data (Soft C-means)

mfuz= 1.26; it=165							
	Clus ter1	Clus ter2	Clus ter3	Clus ter4	Clus ter5	Clus ter6	Total
The right number of data point	15	27	64	20	43	79	248
number of data point wrongly clustered	15	0	3	4	7	0	29
number of data point correctly clustered	0	27	61	16	36	79	219
Accuracy (%)	0	100	95.31	80	83.72	100	88.31

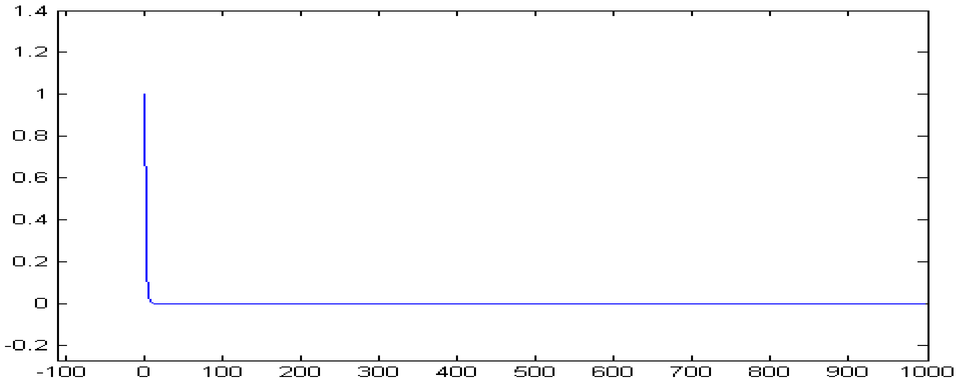


Figure 4.3: SCM Convergence graph for Iris data. X-axis: Number of iteration and Y-axis: Threshold value E

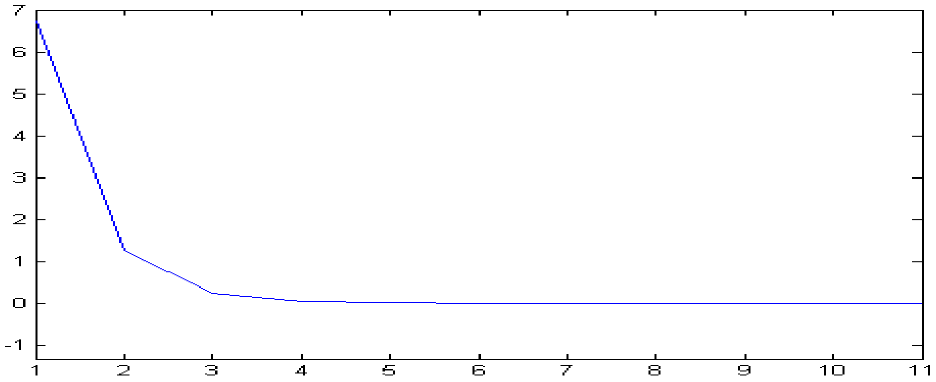


Figure 4.4: SCM Convergence graph for WBCD data. X-axis: Number of iteration and Y-axis: Threshold value E

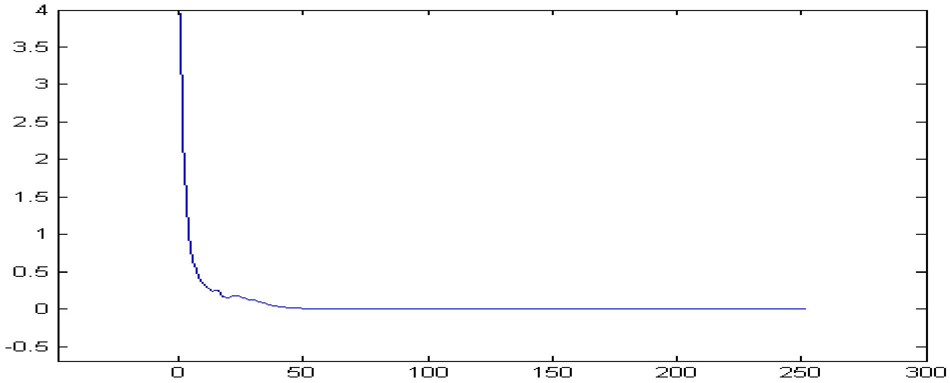


Figure 4.5: Convergence graph for Iyer data. X-axis: Number of iteration and Y-axis: Threshold value E

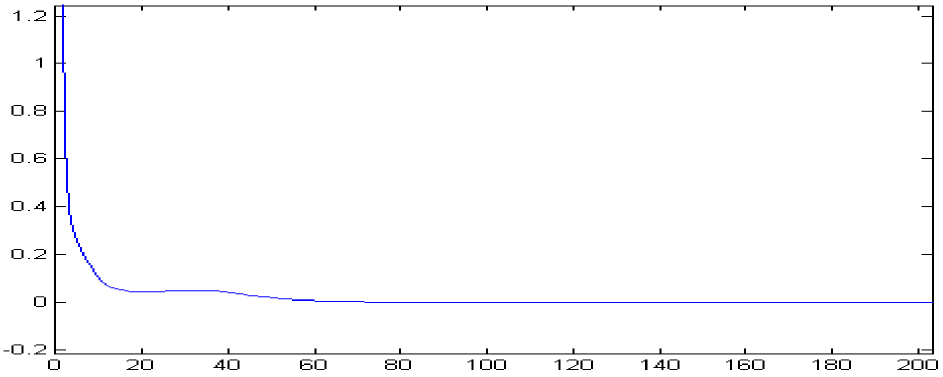


Figure 4.6: Convergence graph for Cho data. X-axis: Number of iteration and Y-axis: Threshold value E

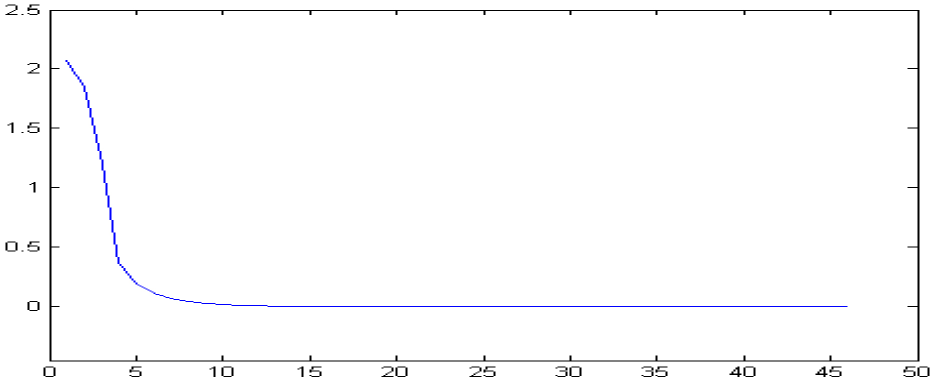


Figure 4.7: Convergence graph for Leukemia data. X-axis: Number of iteration and Y-axis: Threshold value E

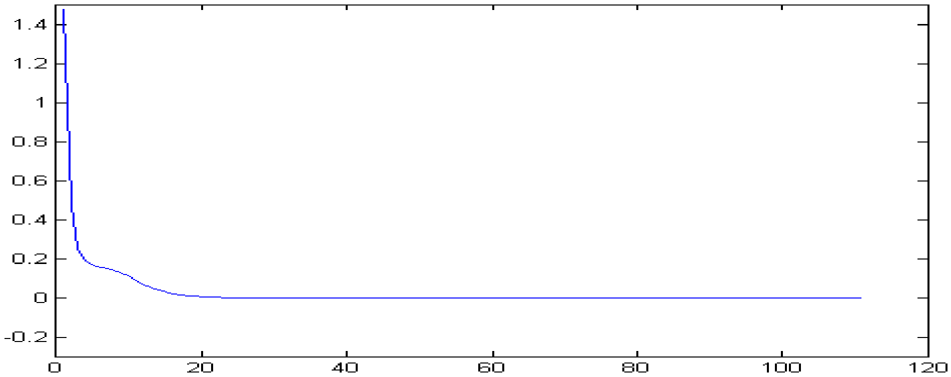


Figure 4.8: Convergence graph for Breast data A. X-axis: Number of iteration and Y-axis: Threshold value E

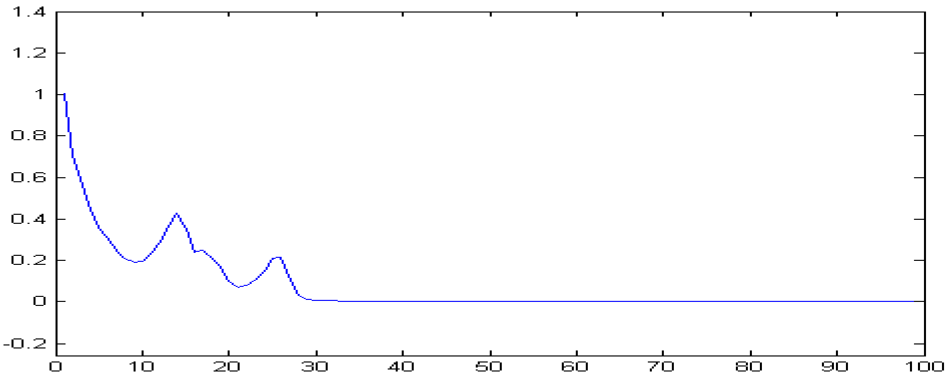


Figure 4.9: Convergence graph for Breast data B. X-axis: Number of iteration and Y-axis: Threshold value E

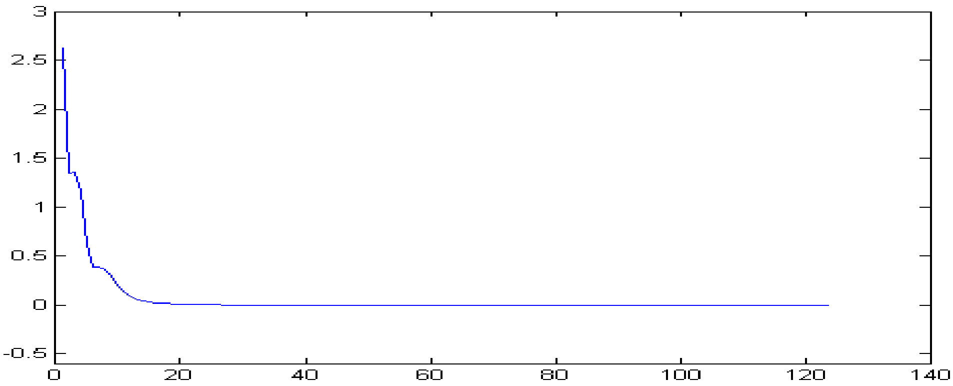


Figure 4.10: Convergence graph for Breast Multi data A. X-axis: Number of iteration and Y-axis: Threshold value E

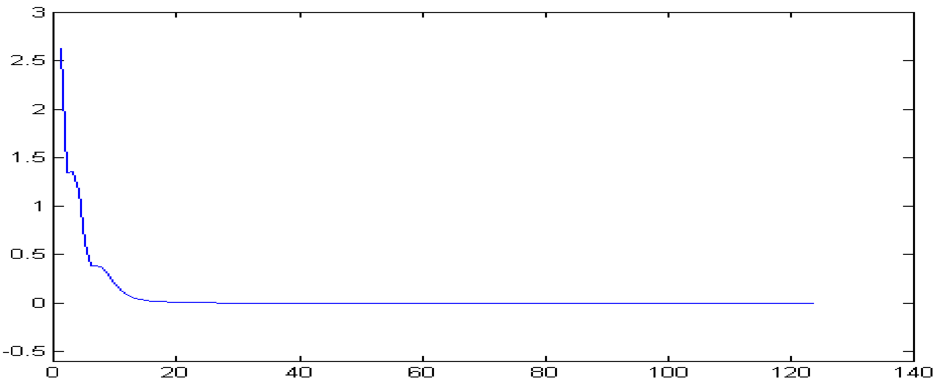


Figure 4.11: Convergence graph for Breast Multi data B. X-axis: Number of iteration and Y-axis: Threshold value E

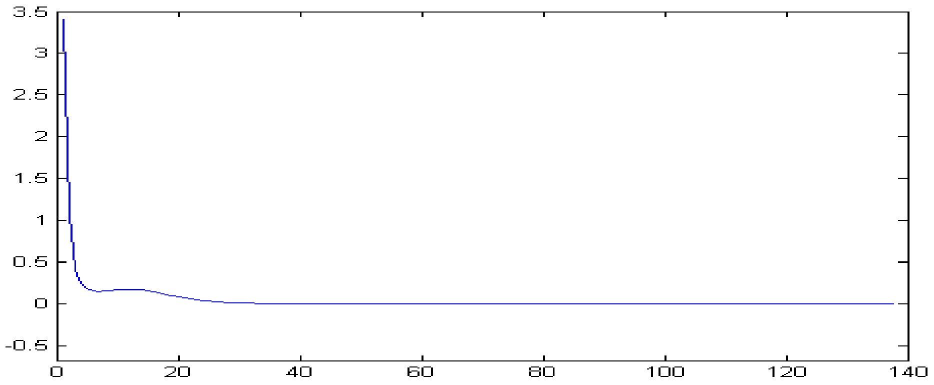


Figure 4.12: Convergence graph for DLBCL A. X-axis: Number of iteration and Y-axis: Threshold value E

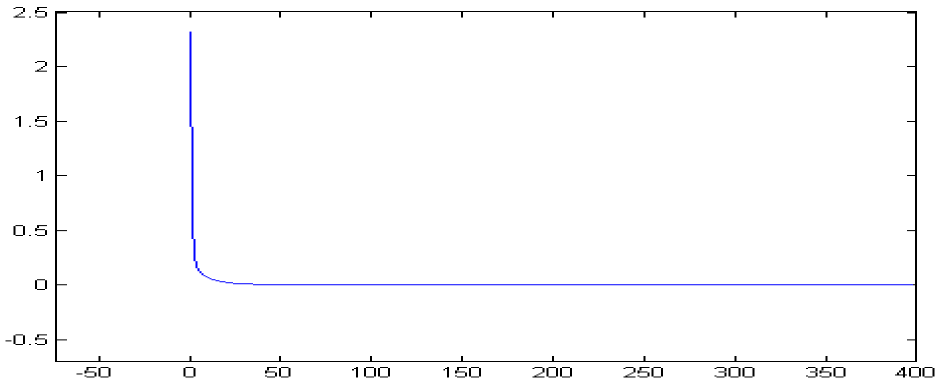


Figure 4.13: Convergence graph for DLBCL B. X-axis: Number of iteration and Y-axis: Threshold value E

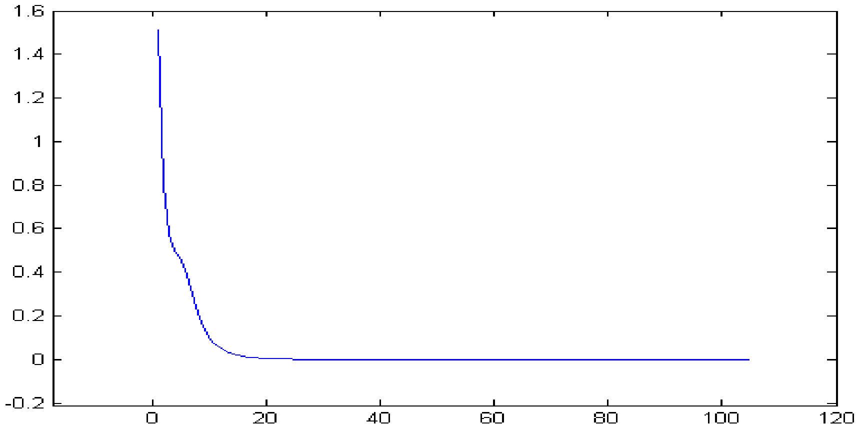


Figure 4.14: Convergence graph for DLBCL C. X-axis: Number of iteration and Y-axis: Threshold value E

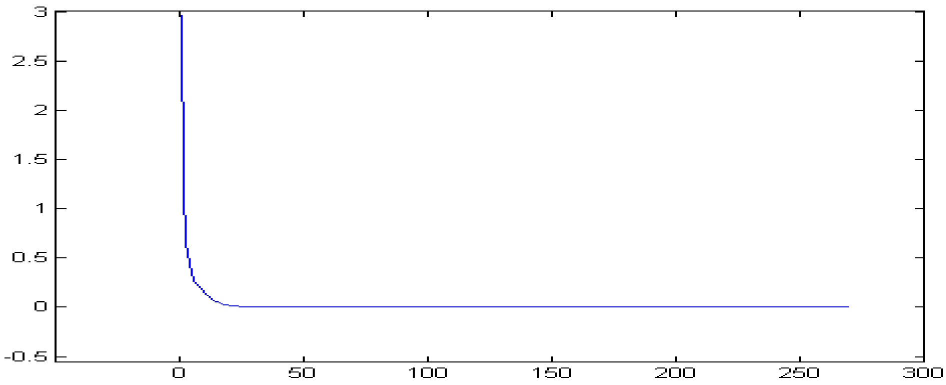


Figure 4.15: Convergence graph for DLBCL D. X-axis: Number of iteration and Y-axis: Threshold value E

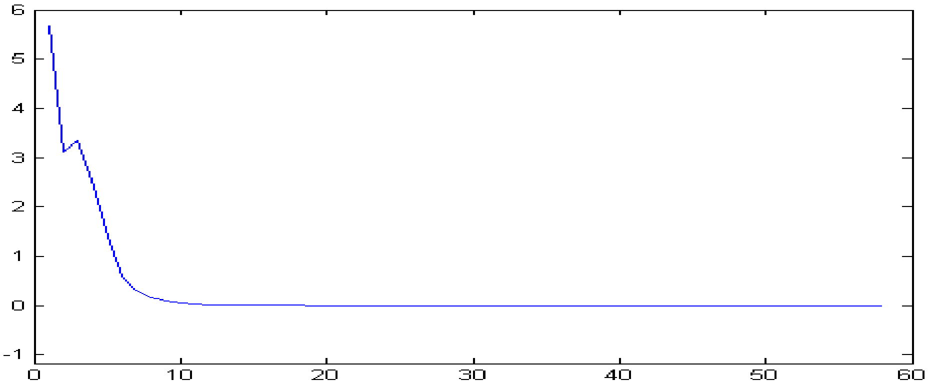


Figure 4.16: Convergence graph for Lung Cancer data. X-axis: Number of iteration and Y-axis: Threshold value E

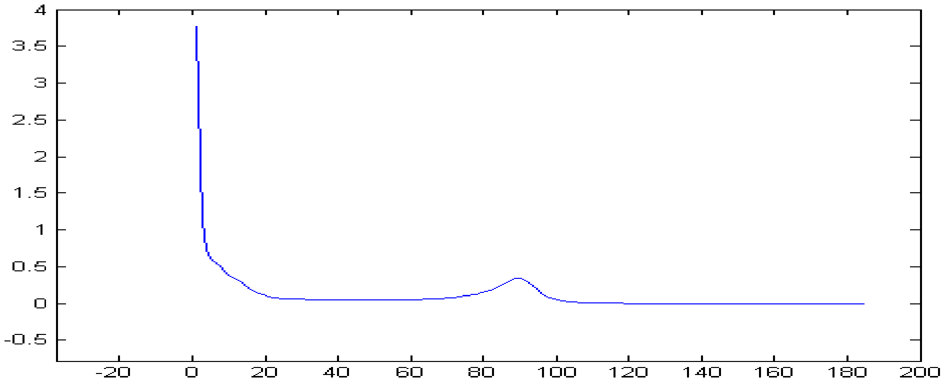


Figure 4.17: Convergence graph for St.Jude Leukemia data. X-axis: Number of iteration and Y-axis: Threshold value E

4.4 Comparative studies on Hard C-means and Soft C-means clustering Algorithm

This section deals with comparative studies on Hard C-means and Soft C-means Clustering algorithm. All the fifteen datasets described in section 4.1.1 has been considered to compare performances of Hard C-means and Soft C-means clustering algorithm.

Table 4.38 shows the result obtained by HCM and SCM clustering algorithm for Iris data. The total count error in case of HCM clustering algorithm was 17 whereas in case of SCM, it was 14. The similar result was also reported in literature [46]. Percentage increase in accuracy for SCM is by 2 %. It may be noted that accuracy of 100 % was achieved for cluster 1 in HCM as well as in case of SCM. Percentage accuracy is increase by 14 % for cluster 3 in case of SCM.

Table 4.39 shows the result for WBCD data. Percentage increase in accuracy for SCM is by 0.30% for WBCD. Total count error in case of HCM is 29, whereas in case of SCM, it is reduced to 27.

Table 4.40 shows the result obtained by HCM and SCM for Serum data (Iyer data). The data point of one clusters are overlapping with other clusters. This is the reason very less accuracy was achieved for this datasets. Number of data point correctly clustered for this datasets is 268 for HCM and 252 for SCM. The optimal value of *m* was chosen as 1.92.

Table 4.41 contains the result for Cho data. Percentage accuracy in case of HCM is 60.88 % whereas in case of SCM, it is 63.47 %. Note that percentage accuracy for cluster 4 is increased by 59.26% (i.e., 72.22 - 12.96), whereas for cluster 3 it is decreased by 26.67%(i.e., 62.67 - 36).

Table 4.42 consists the result for Leukemia data (Golub's data). Accuracy of 59.72 % was achieved in case of HCM and 55.56% in case of SCM. It may be noted that cluster 2 is having equal accuracy (44%) in case of HCM as well as in case of SCM. The Golub et. al.'s microarray datasets is very challenging because the appearance of the two types of acute Leukemia is highly similar in nature. This was the reason much better accuracy was not achieved in this case. One probable solution to deal with this problem could be use dimensionality reduction techniques to reduce the number of features and then subsequently use of SCM clustering algorithm.

Table 4.43 to Table 4.46 consists the result for subtypes of Breast data. As far as Breast data A is concerned, Number of correctly clustered data point has been raised to 86 (SCM) from 71 (HCM) and therefore percentage accuracy increased by 15.31 %. It may be noted that in case of SCM, accuracy of 100 % was achieved for cluster 2 whereas for cluster 1 number of correctly classified data point is zero. In case of Breast data B, percentage accuracy has been increased by 15.32 (i.e., 87.76-72.44)%. It may be noted that 100% of accuracy was achieved for cluster 1 and cluster 3 in case of SCM (Breast data B). In case of Breast multi data A, percentage accuracy is increased by 10.68. It is important to note that cluster 3 achieve 35.71% accuracy in case of Breast multi data B whereas in case of SCM it achieved accuracy upto 92.85%.

Table 4.47 to Table 4.50 consists of the result for subtypes of DLBCL Data. As far as DLBCL A is concerned, increase in accuracy in case of SCM is by 5.67 %. Note that HCM performs better in case of DLBCL B data. Number of data point correctly clustered in case of HCM is 140 whereas 136 in case of SCM. SCM gives optimal accuracy when m is 1.285. As far as DLBCL C and DLBCL D are concerned SCM performs better compared to HCM algorithm on the basis of accuracy parameter. The data of DLBCL B is of highly distinctively separated in nature compared to other DLBCL (A, C, D) and that is the reason higher accuracy was achieved in case of DLBCL B. The reason for inferior performance of SCM compared to HCM for DLBCL B could be solved by finding a better m value.

Table 4.51 shows the result obtained by HCM and SCM for Lung Cancer data. Overall accuracy has been raised by 4 % in case of SCM compared to HCM clustering algorithm. It may be observed that accuracy of cluster 3 is 47.62% whereas in case of SCM it has been raised upto 61.9 %.

Table 4.52 shows the result obtained by HCM and SCM for St. Jude Leukemia data. The data in this case is of highly separable in nature. As far as HCM is concerned 100 percent accuracy was achieved for cluster 2 whereas in case of SCM 100 % accuracy was achieved for cluster 2 as well as cluster 6. It may be noted that the least accuracy was achieved for cluster 5 in HCM as well as in SCM. SCM obtained 16.28 (i,e., 83.72-

67.44) % more accuracy compared to HCM algorithm for Cluster 5.

Table 4.37: Comparative study of HCM and SCM using all fifteen data

Sl. No.	**Datasets**	**# cluster**	**Hard C-means**				**SCM**					
			# Error	Error(%)	# correct	Accuracy (%)	mfuz	# Error	Error (%)	# correct	Accuracy (%)	% Increase In accuracy
1	**Iris**	3	17	11.33	133	88.67	4.2	14	9.33	136	90.67	2
2	**WBCD**	2	29	4.25	654	97.75	1.58	27	3.95	656	96.04	.3
3	**Iyer data/Serum data**	11	249	48.1624	268	51.84	1.92	265	51.26	252	48.74	-3.1
4	**Cho data (yeast data)**	5	151	39.1191	235	60.88	2.15	140	36.27	246	63.73	2.85
5	**Leukemia (Golub Experiment)**	2	29	40.28	43	59.72	1.28	32	44.44	40	55.56	-4.16
6	**Breast data A**	3	27	27.55	71	72.44	1.6	12	12.25	86	87.75	15.31
7	**Breast data B**	4	23	46.93	26	53.06	1.15	17	34.7	32	65.30	12.24
8	**Breast Multi data A**	4	21	20.39	82	79.61	1.3	10	9.71	93	90.29	10.68
9	**Breast Multi data B**	4	15	48.88	17	53.125	1.795	16	50	16	50	-3.125
10	**DLBCL A**	3	66	46.8085	75	53.191	1.40	58	41.14	83	58.86	5.669
11	**DLBCL B**	3	40	22.22	140	77.78	1.285	44	24.44	136	75.56	-2.22
12	**DLBCL C**	4	28	48.28	30	51.7241	1.345	14	24.14	44	75.86	24.14
13	**DLBCL D**	4	74	57.36	55	42.64	1.25	64	49.62	65	50.38	7.74
14	**Lung Cancer**	4	55	27.92	142	72.0812	1.07	47	23.86	150	76.14	4.06
15	**St. Jude Leukemia data**	6	37	14.91	211	85.08	1.26	29	11.69	219	88.31	3.23

Table 4.38: Comparative study on HCM and SCM for Iris

		# data point	**# data point wrongly clustered**	**# data point correctly clustered**	**Accuracy(%)**
HCM	Cluster1	50	0	50	100
	Cluster2	50	4	46	92
	Cluster3	50	13	37	74
	Total	150	17	133	88.67
SCM	Cluster1	50	0	50	100
	Cluster2	50	3	47	94
	Cluster3	50	11	39	88
	Total	150	14	136	90.67

Table 4.39: Comparative study on HCM and SCM for WBCD

		# data point	**# data point wrongly clustered**	**# data point correctly clustered**	**Accuracy(%)**
HCM	Cluster1	444	142	302	68.01
	Cluster2	239	112	127	53.14
	Total	683	254	429	62.81
SCM	Cluster1	444	09	435	97.97
	Cluster2	239	20	219	91.63
	Total	683	29	654	95.75

Table 4.40: Comparative study of HCM and SCM using Serum Data (Iyer Data)

		# data point	# data point wrongly clustered	# data point correctly clustered	Accuracy(%)
HCM	Cluster1	33	17	16	48.48
	Cluster2	100	84	16	16
	Cluster3	145	7	138	95.17
	Cluster4	34	34	0	0
	Cluster5	43	31	12	27.91
	Cluster6	7	6	1	14.29
	Cluster7	34	17	17	50
	Cluster8	14	1	13	92.86
	Cluster9	63	28	35	55.56
	Cluster10	19	12	7	36.84
	Cluster11	25	12	13	52
	Total	517	249	268	51.84
SCM	Cluster1	33	28	5	15.15
	Cluster2	100	6	94	94
	Cluster3	145	69	84	57.93
	Cluster4	34	33	1	2.94
	Cluster5	43	24	19	44.19
	Cluster6	7	7	0	0
	Cluster7	34	17	17	50
	Cluster8	14	14	0	0
	Cluster9	63	41	22	34.92
	Cluster10	19	17	2	10.53
	Cluster11	25	17	8	32
	Total	517	265	252	48.74

Table 4.41: Comparative study on HCM and SCM for Cho Data)

		# data point	# data point wrongly clustered	# data point correctly clustered	Accuracy(%)
HCM	Cluster1	67	30	37	55.22
	Cluster2	135	25	110	81.48
	Cluster3	75	28	47	62.67
	Cluster4	54	47	7	12.96
	Cluster5	55	21	34	61.82
	Total	386	151	235	60.88
SCM	Cluster1	67	15	52	77.62
	Cluster2	135	55	80	59.3
	Cluster3	75	48	27	36
	Cluster4	54	15	39	72.22
	Cluster5	55	8	47	85.45
	Total	386	141	245	63.47

Table 4.42: Comparative study on HCM and SCM for Leukemia Data (Golub Expeiment)

		# data point	# data point wrongly clustered	# data point correctly clustered	Accuracy(%)
HCM	Cluster1	47	15	32	68.09
	Cluster2	25	14	11	44
	Total	72	29	43	59.72
SCM	Cluster1	47	18	29	61.702
	Cluster2	25	14	11	44
	Total	72	32	40	55.56

Table 4.43: Comparative study on HCM and SCM for Breast Data A

		# data point	# data point wrongly clustered	# data point correctly clustered	Accuracy(%)
HCM	Cluster1	11	1	10	90.91
	Cluster2	51	22	29	56.86
	Cluster3	36	4	32	88.89
	Total	98	27	71	72.44
SCM	Cluster1	11	11	0	0
	Cluster2	51	0	51	100
	Cluster3	36	1	35	97.22
	Total	98	12	86	87.76

Table 4.44: Comparative study on HCM and SCM for Breast Data B

		# data point	# data point wrongly clustered	# data point correctly clustered	Accuracy(%)
HCM	Cluster1	12	0	12	100
	Cluster2	11	5	6	54.54
	Cluster3	7	5	2	28.57
	Cluster4	19	13	6	31.58
	Total	49	23	26	53.06
SCM	Cluster1	12	0	12	100
	Cluster2	11	5	6	54.54
	Cluster3	7	0	7	100
	Cluster4	19	12	7	36.84
	Total	49	17	32	65.31

Table 4.45: Comparative study on HCM and SCM for Breast multi data A

		# data point	# data point wrongly clustered	# data point correctly clustered	Accuracy(%)
HCM	Cluster1	26	2	24	92.31
	Cluster2	26	1	25	96.15
	Cluster3	28	18	10	35.71
	Cluster4	23	0	23	100
	Total	103	21	82	79.61
SCM	Cluster1	26	5	21	80.77
	Cluster2	26	1	25	96.15
	Cluster3	28	2	26	92.85
	Cluster4	23	2	21	91.3
	Total	103	10	93	90.291

Table 4.46: Comparative study on HCM and SCM for Breast multi data B

		# data point	**# data point wrongly clustered**	**# data point correctly clustered**	**Accuracy(%)**
HCM	Cluster1	5	3	2	40
	Cluster2	9	2	7	77.78
	Cluster3	7	3	4	57.14
	Cluster4	11	7	4	36.36
	Total	32	15	17	53.13
SCM	Cluster1	5	3	2	40
	Cluster2	9	3	6	66.67
	Cluster3	7	4	3	42.86
	Cluster4	11	6	5	45.45
	Total	32	16	16	50

Table 4.47: Comparative study on HCM and SCM for DLBCL A

		# data point	**# data point wrongly clustered**	**# data point correctly clustered**	**Accuracy(%)**
HCM	Cluster1	49	26	23	46.94
	Cluster2	50	22	28	56
	Cluster3	42	18	24	57.14
	Total	141	66	75	53.19
SCM	Cluster1	49	18	31	63.27
	Cluster2	50	23	27	54
	Cluster3	42	17	25	59.52
	Total	141	58	83	58.87

Table 4.48: Comparative study on HCM and SCM for DLBCL B

		# data point	**# data point wrongly clustered**	**# data point correctly clustered**	**Accuracy(%)**
HCM	Cluster1	42	18	24	57.14
	Cluster2	51	7	44	86.27
	Cluster3	87	15	72	82.76
	Total	180	40	140	77.78
SCM	Cluster1	42	13	29	69.05
	Cluster2	51	16	35	68.63
	Cluster3	87	15	72	89.66
	Total	180	44	136	75.56

Table 4.49: Comparative study on HCM and SCM for DLBCL C

		# data point	**# data point wrongly clustered**	**# data point correctly clustered**	**Accuracy(%)**
HCM	Cluster1	17	1	16	94.11
	Cluster2	16	9	7	43.75
	Cluster3	13	12	1	7.69
	Cluster4	12	6	6	50
	Total	58	28	30	51.72
SCM	Cluster1	17	4	13	76.47
	Cluster2	16	6	10	62.5
	Cluster3	13	7	6	46.15
	Cluster4	12	9	3	25
	Total	58	26	32	55.17

Table 4.50: Comparative study on HCM and SCM for DLBCL D

		# data point	**# data point wrongly clustered**	**# data point correctly clustered**	**Accuracy(%)**
HCM	Cluster1	19	13	6	31.58
	Cluster2	37	28	9	24.32
	Cluster3	24	13	11	45.83
	Cluster4	49	20	29	59.18
	Total	129	74	55	42.64
SCM	Cluster1	19	8	11	57.9
	Cluster2	37	19	18	48.65
	Cluster3	24	10	14	58.33
	Cluster4	49	27	22	44.89
	Total	129	64	65	50.39

Table 4.51: Comparative study on HCM and SCM for Lung Cancer

		# data point	**# data point wrongly clustered**	**# data point correctly clustered**	**Accuracy(%)**
HCM	Cluster1	139	42	97	69.78
	Cluster2	17	1	16	94.11
	Cluster3	21	11	10	47.62
	Cluster4	20	1	19	95
	Total	197	55	142	72.08
SCM	Cluster1	139	36	103	74.1
	Cluster2	17	2	15	88.24
	Cluster3	21	8	13	61.9
	Cluster4	20	1	19	95
	Total	197	47	150	76.14

Table 4.52: Comparative study on HCM and SCM for St. Jude Leukemia Data

		# data point	**# data point wrongly clustered**	**# data point correctly clustered**	**Accuracy(%)**
HCM	Cluster1	15	15	0	0
	Cluster2	27	0	27	100
	Cluster3	64	3	61	95.31
	Cluster4	20	4	16	80
	Cluster5	43	14	29	67.44
	Cluster6	79	1	78	98.73
	Total	248	37	211	85.08
SCM	Cluster1	15	15	0	0
	Cluster2	27	0	27	100
	Cluster3	64	3	61	95.31
	Cluster4	20	4	16	80
	Cluster5	43	7	36	83.72
	Cluster6	79	0	79	100
	Total	248	29	219	88.31

4.5 Conclusion

The SCM based clustering algorithm is a distinct improvement from the conventional HCM clustering algorithm. Its ability to cluster independent of the data sequence provides a more stable clustering result. Computer simulation shows that Soft C-means performs superior compared to Hard C-means algorithm in eleven cases out of fifteen cases. Datasets belonging to these cases are Iris, WBCD, Yeast (Cho) data, Breast Data (A, B), Breast multi data A, DLBCL (A,C,D), Lung Cancer and St. Jude leukemia. Whereas Hard C-means shows superior performance in four cases. Datasets belonging to these cases are serum data, leukemia data, Breast multi data B and DLBCL B. As seen from the experiments, the SCM based clustering algorithm was able to provide the highest accuracy and generalization results.

Chapter 5

Genetic Algorithm based Clustreing Algorithm

Clustering can be formally formulated as a NP-hard grouping problem from optimization perspective [102]. This research finding has stimulated the search for efficient approximation algorithms, including not only the use of ad-hoc heuristics for particular classes or instances of problems, but also the use of general-purpose metaheuristics [103]. Particularly, evolutionary algorithms are metaheuristics widely believed to be effective on NP-hard problems, being able to provide near-optimal solutions to such problems in reasonable time. Under this assumption, a large number of evolutionary algorithms for solving clustering problems have been proposed in the literature . A useful review on this can be found from review paper [34]. These algorithms are based on the optimization of some objective function (i.e., the so-called, fitness function) that guides the evolutionary search. In evolutionary algorithm, Genetic Algorithm (GA) becomes natural choice for cluster formation algorithm due to its wide applicability in wide range of areas.

GA is inspired by Darwin's theory of evolution. A GA works with a population of individuals each of which represents a potential solution to the problem to be solved. A typical individual is a binary string on which the problem solution is encoded. Problem representation is one of the key decision to be made when applying a GA to a problem. Problem representation in a GA individual determines the shape of the solution space, that a GA must search. As a result, "*different encodings of the same problem are essentially different problems for a GA*" [104]. The application of GAs for solving problems of pattern recognition appears to be appropriate and natural. A number of research articles in this area have started to come out [105], [106], [107], [108], [109], [110], [111], [112], [113], [114]. An application of GAs has been reported in the area of (supervised) pattern classification for designing a GA-classifier [107], [115]. GA based Clustering algorithm for machine learning data has been also reported in literature [17], [116], [117], [118]. The paper [17] was the referenced which motivated us to work on GA based clustering algorithm.

In the paper [17], extensive studies has been done on wide variety of artificial and real-life data. These datasets having both overlapping and non-overlapping class boundaries. Paper [17] discusses binary as well as multi-class classifier problem (unsupervised). The paper [17] is specific to pattern recognition data. Mean square error (MSE) has been used as fitness function in paper [17]. In paper [17], chromosome representation is based on cluster center which is made up of features of the data point (i.e., gene). When no. of features considered are large e.g., microarray data, length of the chromosome becomes very large if chromosome representation was followed based on paper [17]. In such cases it is advisable to go for some alternative means of chromosome representation e.g., based on instances i.e., data point itself instead of going for feature based representation. The paper [17] is specific to pattern recognition data. There are no work reported in literature for bioinformatics data specially for microarray data using GA. In this chapter of the thesis, study has been made on Family of GA based clustering algorithm to bioinformatics data. Bioinformatics data possess some characteristics feature which machine learning data do not possess. Microarray data possesses a number of features (generally, in range of $10^3 - 10^4$) very large compared to pattern recognition data.

In this thesis, along with paper [17], three different representation schemes for GA based clustering was studied. This chapter of the thesis deals with machine learning data as well as bioinformatics data having overlapping and non-overlapping clusters. The data belongs to binary as well as multi class problem. It also deals with problem like clusters within a clusters (i.e., subtypes of a cluster). Binary representation (SGA-simple Genetic Algorithm) as well as floating-point representation (RGA-Real coded Genetic Algorithm) has been considered for GA. It is important to note that efficiency of a GA based algorithm mainly depends on two factors; first representation scheme and fitness function computation [137], [138]. Depending upon chromosome representation schemes crossover and mutation operator was modified. The way chromosome was represented and novel fitness function was used in this thesis makes it different from previous approaches and results in an efficient clustering algorithm.

5.1 Basic principle

The searching capability of GAs [139] has been used in this chapter of the thesis for cluster formation of 'n' data points where labeled information are not available at the time of cluster formation. This has been achieved using either determining 1): Data point belonging to each cluster i.e., $\{V_1, V_2 \ldots, V_C\}$ or 2): Cluster center i.e., $\{v_1, v_2 \ldots, v_C\}$ in problem solution space R^N ; where 'C' is a fixed number of cluster given by user. The fitness function that has been adopted is the HS_Ratio of the cluster. HS_Ratio has been discussed in detail in section 5.2.3.

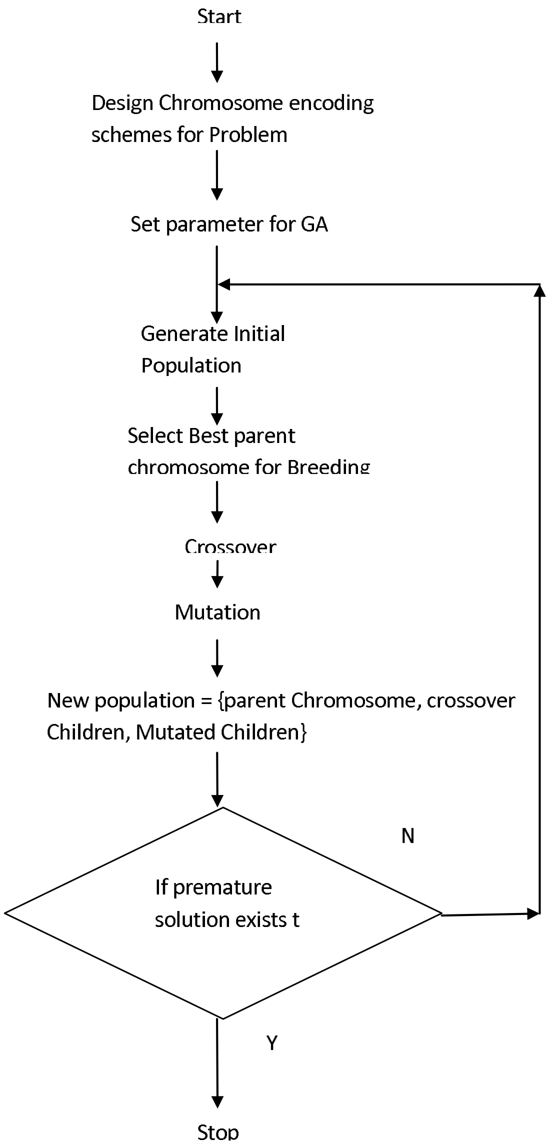
The objective of the GA is to search for the appropriate 1:) Cluster i.e., $\{V_1, V_2 \ldots, V_C\}$ or 2): Cluster center i.e, $\{v_1, v_2 \ldots, v_C\}$; such that fitness function 'f' is minimized.

5.2 Basic Steps involved in GA based Clustering

The basic steps of GAs (shown in fig. 5.1); which are also followed in the GA-clustering algorithm, are now described in details in this section.

Initially, a random population is created, which represents different data point in a cluster or cluster center in the problem search space. Then fitness value of each chromosome is computed. Based on the principle of survival of the fittest, a few of the chromosome are selected and each is assigned a number of copies that go into the mating pool. Then crossover operator are applied on these string and that results in set of crossover children. Next, mutation was applied on the crossover children that results set of mutated children. parent chromosome, crossover children and mutated children yields set of chromosome for the new generation. The process of selection, crossover and mutation continues for a fixed number of generation or till a termination condition is satisfied. In this section; discussion has been made on four different representation schemes for

Figure 5.1: Flow chart of simple GA


Start
Design Chromosome encoding schemes for Problem
Set parameter for GA
Generate Initial Population
Select Best parent chromosome for Breeding
Crossover
Mutation
New population = {parent Chromosome, crossover Children, Mutated Children}
If premature solution exists t
N
Y
Stop

```
Set parameters for the GA;
generation:=1
Initial population with random binary strings;
while generation ≤ max_ generation do
    Evaluate the fitness of all individuals;
    Find the best individual;
    for i=1 to population_size do
        Perform tournament selection;
        Perform crossover and mutation;
    endfor
    Copy the offspring into new population;
    Reproduce the best parent into a random slot;
    Check the convergence of the new population;
    If premature then
        Reproduce the best individual;
        Regenerate other individuals randomly;
    endif
    generation:=generation+1:
endwhile
```

encoding of a chromosome.

5.2.1 Encoding of Chromosome

1. **Representation 1 (GA-R1)**:

   This representation is based on number of data points. In this representation; each chromosome is represented by a sequence of binary numbers representing the clusters. For 'n' data-point of N-dimensional space and 'C' number of clusters, the length of a Chromosome will be '$n \times C$' word length, where the first 'n' word length represents the first cluster, the next 'n' word length represents those of the second cluster, and so on. It may be noted that in a cluster if a word position is '1' (It is said to be in ON state), it means that the data point is present and '0' (it is said to be in OFF state) means data point is absent. As an illustration for the above representation, let us consider the following example.

   Example 1.

   Let us consider Iris data [150 x 4], where n=150, N=4 and C=3, i.e., the space is four dimensional and the number of clusters being considered is three. Therefore, the size of the Chromosome will be 450 (i.e., $n \times C$). Then the Chromosome/String representation will be as follows:

Encoding of chromosome using representation 1		
First Cluster	Second Cluster	Third Cluster
1 0 0 0 0 1 . . . upto 150 bits	0 1 1 0 0 0 . . . upto 150 bits	0 0 0 1 1 0 . . . upto 150 bits

   According to above chromosome representations: since in first cluster index 1 and 6 are one. Therefore, Data point '1' and Data point '6' are present in First Cluster. Similarly, Second Cluster contains Data point '2' and Data point '3', Third Cluster contains Data point '4' and Data point '5', and so on.

2. **Representation 2 (GA-R2):**

   This representation is based on cluster center (i.e., number of features). In this representation; each Chromosome is represented by a sequence of real numbers representing the centers of 'C' clusters. For 'n' data-point of N-dimensional space, the length of a Chromosome will be ‘$N \times C$’ word length, where the first ‘N’ positions (or, features) represent the ‘$center\ of\ first\ cluster$‘, next ‘$N$’ positions represent those of the ‘$center\ of\ second\ cluster$‘, and so on. It may be noted that cluster center is of N-dimensional space. This representation is similar to paper [17]. As an illustration for the above representation, let us consider the following example.

Example 2.

Consider the same Iris data again. The size of the Chromosome in this case will be twelve (i.e., $N \times C = 12$). Then the Chromosome/String representation will be:

Encoding of chromosome using representation 2		
Center of First Cluster	Center of Second Cluster	Center of Third Cluster
5.2 4.1 1.5 0.1	5.3 3.7 1.5 0.2	5.7 2.9 4.2 1.3

3. **Representation 3 (GA-R3):**

This representation is extension of ‘Representation 2’. This involves two step: In first step, a chromosome is represented as stated in Representation 2 and in second step; each word of first step representation is represented by a sequence of binary length of specified length (say, ‘*nw*’). The minimum value of ‘*nw*’ is equal to size of binary number required to represent the maximum value of a feature in original data.

Example 3: Consider the same Iris data again. In first step, a chromosome will be size of 12 word length (according to Representation 2). Here each word (feature) is represented by a real number. In the second step, each word of representation 2 is represented by a sequence of binary number of specified word length. Let us take 10 word length to represent one word (i.e., one feature) of first step representation. Therefore the resultant length of a Chromosome after second representation will be of ‘120’ word length (i.e., $3 \times 4 \times 10 = 120$). Then the Chromosome/String representation will be :

Consider the Center of First Cluster

Encoding of chromosome using representation 3		
Center of First Cluster	Center of Second Cluster	Center of Third Cluster
1 0 0 0 0 1 . . . Upto 40 bits	0 1 1 0 0 0 . . . Upto 40 bits	0 0 0 1 1 0 . . . Upto 40 bits

Complete view of first cluster of chromosome using representation 3			
1 1 1 1 0 0 0 0 1 1	1 1 1 1 1 0 0 0 0 0	0 0 0 0 0 1 1 1 1 1	1 1 0 0 1 1 0 0 1 1

First block of the first cluster (i.e. first 10 bits of the first cluster) represents one gene i.e., the feature number one i.e. first dimension of center of first cluster.

4. **Representation 4 (GA-R4):**

This representation is combination of Representation 1 and Representation 3. In first step, chromosome is represented as stated in representation 1. Hence for Iris data, the size of chromosome in first step will be 450 (i.e., 3×150). It's a binary representation. Here if a bit is found to be '1', it means a data point is present in the cluster otherwise the data point is absent in the cluster. Now for each cluster, center (or, mean) was computed. Since center's of each cluster is of dimension four. So now the size of chromosome will be of size 12 (i.e., 3×4). In the next step, each feature of cluster's center is represented by binary sequence of specified length (say, 10) as stated in Representation 3. So the size of resultant chromosome will be 120 (i.e., $3 \times 4 \times 10 = 120$) word (or, bit) length. Then the Chromosome/String representation will be:

Encoding of chromosome using representation 4		
First Cluster	Second Cluster	Third Cluster
1 0 0 0 0 1 . . . Upto 40 bits	0 1 1 0 0 0 . . . Upto 40 bits	0 0 0 1 1 0 . . . Upto 40 bits

It is important to note that Representation 4 is equivalent to 'representation 3'; but the way it is derived i.e., the meaning is different. Hence the simulation result obtained for this two representation will be same if the randomly initial population (i.e., cluster) generated are same. For this reason the discussion has been made on the simulation result obtained by representation 3 only in this chapter.

5.2.2 Population initialization

The 'C' number of clusters encoded in each chromosome are initialized as stated in Encoding of chromosome (Section 5.2.1). The chromosome initialization can be done either randomly or by using any greedy or intelligent method. This process is repeated for each of the 'P' chromosome in the population, where 'P' is the size of the population.

5.2.3 Fitness Evaluation of Chromosome

This is the one of the most important part of proposed approach. The fitness function evaluation is based on Homogeneity and separation value. It is based on the principle *"objects within one cluster are assumed to be similar to each other, while objects in different clusters are dissimilar"*. Fitness computation process consists of two steps: in first step, Homogeneity value and Separation value is calculated. In second step, HS_Ratio is defined as ratio of homogeneity to separation.

The homogeneity of a cluster V is defined as follows ([20], [45]):

$$H_1(V) = \frac{\sum_{E_i,\ E_j \in V,\ E_i \neq E_j} Similarity\left(E_i\ ,\ E_j\right)}{\parallel V \parallel . (\parallel V \parallel -1)}$$

This definition represents the homogeneity of cluster V by the average pair-wise object similarity within V.

Cluster separation is analogously defined from various perspectives to measure the dissimilarity between two clusters V_1, V_2 ([20], [45]). For example:

$$S_1(V_1,V_2) = \frac{\sum_{E_i \in V_1,\ E_j \in V_2} Similarity\left(E_i\ ,\ E_j\right)}{\parallel V_1 \parallel . (\parallel V_2 \parallel)}$$

Since these definitions of homogeneity and separation are based on the similarity between objects, the quality of V increases with *higher homogeneity values within V and lower separation values between V and other clusters*. Once homogeneity of a cluster and the separation between a pair of clusters has been defined, for a given clustering result $\{V_1, V_2, \ldots, V_C\}$, Then average homogeneity and the average separation of V can be defined. For example, Shamir et al. [20] used definitions of

$$H_{average} = \frac{\sum_{V_i \in V} \parallel V_i \parallel . H_1(V_i)}{N}$$

and

$$S_{average} = \frac{1}{\sum_{V_i \neq V_j} \| V_i \| . \| V_j \|} \sum_{V_i \neq V_j} \| V_i \| . \| V_j \| . S_1(V_1, V_2)$$

to measure the average homogeneity and separation for the set of clustering results V. The HS_Ratio is defined as : $HS\_Ratio = \frac{H_{average}}{S_{average}}$. The fitness function J for a chromosome is defined as: $J = 1/HS\_Ratio$. Here objective is to minimize fitness function J.

5.2.4 Selection

The selection step in GA, selects chromosome from the mating pool and follows *"the survival of the fittest"* concept of Darwin's natural genetic system. In this chapter, a proportional selection strategy has been adopted. Roulette Wheel selection is one common technique that implements the proportional selection strategy. According to this, a chromosome is being assigned with a number of copies, which is proportional to its fitness in the population that goes into the mating pool for further genetic operations [139].

5.2.5 Crossover

It is a type of genetic operations, which is used to create new child chromosome from parent chromosome after exchanging information between them. It is based on probabilistic model. Several variants of Cross-over has been discussed in past [139]. In this thesis, a single-point crossover with a fixed crossover probability 'Pc' is used. For chromosome of length 'cs', a random integer 'cp', called the crossover point, is generated in the range [2, cs-1]. The portions of the chromosome lying to the right of the crossover point are exchanged to produce two offspring. It is important to note that depending upon the representation schemes of chromosome in GA crossover operation changes. GA-R2 and GA-R3 follows crossover as stated above whereas in case of GA-R1, after doing the crossover as stated above, a post processing is required. Details about this post processing is explained below:

1. Crossover in GA-R1

   Let us consider a dataset having ten data points of two dimension and number of cluster is two. According to GA-R1, chromosome representation will be as follows:

Chromosome 1	1 0 1 0 1 0 0 0 1 1 0 1 0 1 0 1 1 1 0 0
Chromosome 2	0 0 1 1 1 0 1 1 0 0 1 1 0 0 0 1 0 0 1 1

crossover point ‘*cp*’ is 10. Then chromosome after crossover will look like as follows:

Crossover children 1 (Chromosome)	1 0 1 0 1 0 0 0 1 1 1 1 0 0 0 1 0 0 1 1
Crossover children 2 (Chromosome)	0 0 1 1 1 0 1 1 0 0 0 1 0 1 0 1 1 1 0 0

Now let us consider crossover children 1; cluster 1 contains data point {1 3 5 9 10} and cluster 2 contains data point {1 2 6 9 10}. It may be noted that crossover children's '1' do not follow definition of clustering defined in section 2.2.1. data points {1 9 10} appear in both the cluster and data points {4, 7, 8} is missing in chromosome (crossover children 1) i.e., these data point do not belong to any cluster. To sort out this problem, post processing is required for each and every crossover children and it is done as follows:

Select any cluster in a chromosome randomly and fix that as a true cluster and make changes to other cluster such that it follows definition of clustering.

For illustration, consider crossover children 1 as an example. select any cluster randomly out of available two clusters. say cluster 1 has been chosen. Make this as true cluster and do processing in cluster 2 in such a way that it follows definition of clusters. After processing, crossover children 1 look like as follows:

Crossover children 1 (Chromosome)	1 0 1 0 1 0 0 0 1 1 0 1 0 1 0 1 1 1 0 0

After post processing, cluster 1 contains data point {1 3 5 9 10} and cluster 2 contains data point {2 4 6 7 8} which follows definition of clustering.

5.2.6 Mutation

It is a type of genetic operator that alters one ore more gene values in a chromosome from its initial state. This can result in entirely new gene values being added to the gene pool. With these new gene values, the genetic algorithm may be able to arrive at better solution than was previously possible. Mutation is an important part of the genetic search as help helps to prevent the population from stagnating at any local optima. Each chromosome in a population undergoes mutation with a fixed probability, 'P_m'. For binary representation of a chromosome (GA-R1 and GA-R3), mutation is done by flipping its bit position (or gene) value i.e. if a bit position is 1 it is made 0 and vice versa. A bit position in GA-R1 represents weather a data point is present in a cluster or not whereas in a GA-R3 it represents a position of cluster center. It is important to note that GA-R1 requires post processing as similar to how it has been done in case of crossover, whereas GA-R3 does not require any processing after mutation. For floating-point representation in GA-R2, mutation was done as follows [17] : A random number η in the range [0, 1] is generated with uniform distribution. If the value at a gene position is 'v', after mutation, it becomes $v \times (1 + 2 \times \eta)$. One may note in this context, that similar sort of mutation operators for real coding have been used mostly in the realm of evolutionary strategies [17].

5.2.7 Termination criterion

In this chapter the processes of fitness computation, genetic operation is executed for a maximum number of iterations.

In the next section, GA based clustering algorithm has been discussed for machine learning data as well as bioinformatics data.

5.3 Experimental Setup

To validate the feasibility and performance of the GA based clustering algorithm, clustering accuracy was used as cluster validation metric. Since the data possess class label information. *Clustering accuracy* is defined as follows:

$Clustering\ Accuracy = (\frac{Number\ of\ Correct\ Count}{Total\ number\ of\ instances\ genes/samples}) \times 100.$

Simulation studies has been carried out in MATLAB 7.0 (Intel C2D processor, 2.0 GHz, 2 GB RAM) and applied it to machine learning data as well as to bioinformatics data. For simplicity, this section is divided into two subsection. First section contains the details result obtained on machine learning data using GA clustering algorithm and second section contains detailed result obtained for bioinformatics data using the same algorithm.

5.3.1 Experiment 1: Machine Learning Data

In this section, discussion has been made on *Family of GA based Clustering algorithm* to two machine learning data i.e., Iris and WBCD. The details of these two data have been already explained in section 4.1.1. Comparison has been done on proposed GA based clustering algorithm with following five standard conventional Clustering algorithm [9] for Iris data:

1. Hierarchical Clustering
2. Self Organizing Map based (SOM) Clustering
3. Hard C-means Clustering
4. Generalized Linear Vector Quantization (GLVQ) Clustering
5. Soft C-means (SCM) Clustering

5.3.2 Results and Discussion

The parameters used for Iris and WBCD data in GA based clustering algorithm is shown in Table 5.1.

Complete result of GA based clustering algorithm for machine learning and bioinformatics data has been given in appendix F. Appendix F contains the details of data point wrongly clustered in GA clustering algorithm. From this, It can be deduce about details of data point correctly clustered in each cluster and subsequently distribution of data point after simulation of cluster formation algorithm. Here in this section, result obtained for GA based clustering algorithm for machine learning data has been presented in brief.

Table 5.2 summarizes result of nine clustering algorithm (5 conventional and 4 GA based clustering) for Iris data. Here best case analysis has been considered for four representation schemes used for GA based clustering algorithm. It may be noted that *"for Iris data a clustering algorithm which gives less than 18 count errors considered* *to be a good clustering algorithm"* [46], [47], [49], [48]. Count error was achieved in the range $\{0 - 10\}$ for GA-clustering Algorithm. It can be easily infer from Table 5.2 that GA based clustering algorithm performs better than all other algorithm for Iris data. GA-R1 achieves accuracy upto 93.33 % and GA-R2 achieves accuracy upto 96%. It is important to note that GA-R3 clustering algorithm can achieve 100 percent accuracy in its best case analysis. It can be easily infers from the Table 5.2 that GA based clustering algorithm performs better than other non-GA based clustering algorithm for Iris data.

Table 5.3 describes the result obtained by GA-R1. It shows the initial cluster distribution (randomly taken from initial population) as well as final cluster distributions after simulation. Total count error was achieved as 10 and therefore percentage accuracy as 93.33%.

Table 5.4 describes the details of result obtained by GA clustering algorithm. It contains following information:

the total number of data points in each cluster in a data, number of data point wrongly clustered, number of data point correctly clustered, details of data point wrongly clustered, individual accuracy of each cluster as well as over all accuracy for GA-R1 for Iris data. Here clustering accuracy result for Iris-setosa is 100 percent, whereas in case of Iris-versicolor and Iris-virginica data, number of data points wrongly clustered is 1 and 9 respectively. Datapoint $\{78\}$ which should be in Iris-versicolor is wrongly clustered into Iris-virginica and data-point $\{102, 107, 114, 120, 122, 134, 139, 143, 147\}$ which should be in Iris-virginica is wrongly classified into Iris-versicolor.

Table 5.5 show the details of the cluster obtained before and after GA run. Table 5.6 describes the result obtained by GA-R2 based genetic algorithms. Count error has been obtained as 6. Accuracy of 100 % was achieved for cluster Iris-setosa and Iris-versicolor, whereas for Iris-virginica 88% accuracy was achieved. The wrongly clustered data points are $\{101, 102, 103, 104, 105, \text{and } 107\}$. In actual practice, all these data points belong to Iris-virginica, but they have wrongly clustered into Iris-versicolor. Another very important point to be noted is that data point $\{102, 107\}$ is wrongly clustered by both representation R1 and R2. These data point are highly non-separable. Data point 102 is having feature value $\{5.8, 2.7, 5.1, 1.9\}$ and Data point 107 is having feature value {4.9, 2.5, 4.5, 1.7}; these data points which are in Iris-virginica are having value similar to data point belonging to Iris-versicolor. This is the reason these data points are wrongly classified/clustered by many algorithm in the literature [47], [49]. Table 5.7 describes the result obtained by representation 3 based genetic algorithms. It shows the details of the generated cluster before as well as after GA run. In this 100% accuracy was achieved.

GA based clustering algorithm (i.e., GA-R1, GA-R2 and GA-R3) was simulated 20 times. Summary of results obtained after simulation has been shown in Table 5.8.

Table 5.1: Parameter used in GA based clustering Algorithm for Pattern recognition data

Parameter	Value
Population Size	10 - 100
Maximum No. Of Iteration	15 - 50
Crossover Probability	0.6 - 0.8
Mutation Probability	0.001 - 0.01

Table 5.2: Comparison of Results for nine clustering algorithm using Iris Data

Algorithm	**Count Error**	**Percentage error**	**Percentage Accuracy**
Hierarchical	48	32	68
SOM	22	14.67	85.33
HCM	17	11.33	88.67
GLVQ	16	10.76	89.33
SCM	14	9.33	90.67
GA(Representation 1)	10	6.67	93.33
GA(Representation 2)	6	4	96
GA(Representation 3)	0	0	100
GA(Representation 4)	0	0	100

Table 5.3: Initial and final cluster distribution for GA-R1 for Iris Data

Initial cluster		
Cluster 1	Cluster 2	Cluster 3
1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28 29 30 31 32 33 34 35 36 37 38 39 40 41 42 43 44 45	53 78 101 103 104 105 106 108 109 110 111 112 113 116 117 118 119 121 123 125 126 129 130 131 132 133 135 136 137 138 140 141 142 144 145 146 148 149	51 52 54 55 56 57 58 59 60 61 62 63 64 65 66 67 68 69 70 71 72 73 74 75 76 77 79 80 81 82 83 84 85 86 87 88 89 90 91 92 93 94 95 96 97 98 99 100 102 107 114 115 120 122 124 127 128 134 139 143 147 150
Final Cluster		
Cluster 1	Cluster 2	Cluster 3
1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28 29 30 31 32 33 34 35 36 37 38 39 40 41 42 43 44 45 46 47 48 49 50	51 52 53 54 55 56 57 58 59 60 61 62 63 64 65 66 67 68 69 70 71 72 73 74 75 76 77 79 80 81 82 83 84 85 86 87 88 89 90 91 92 93 94 95 96 97 98 99 100	101 103 104 105 106 108 109 110 111 112 113 115 116 117 118 119 121 123 124 125 126 127 128 129 130 131 132 133 135 136 137 138 140 141 142 144 145 146 148 149 150
Count error= 10		
Accuracy = 93.33 %		

Table 5.4: Result of GA-R1 using Iris Data

	Iris-setosa	**Iris-versicolor**	**Iris-virginica**	**Total**
The right number of data point	50	50	50	150
Details of Data points wrongly clustered	NIL	78	102 107 114 120 122 134 139 143 147	78 102 107 114 120 122 134 139 143 147
number of data point wrongly clustered	0	1	9	10
number of data point correctly clustered	50	49	41	140
Accuracy (%)	100	98	82	93.33

Table 5.5: Initial and final cluster distribution for GA-R2 for Iris Data

Initial cluster		
Cluster1	Cluster2	Cluster3
1 2 5 11 13 17 21 22 25 29 32 35 39 44 45 50 59 60 61 71 72 73 74 75 76 77 78 79 86 90 98 99 46 49 121 122 123 124 125 126 127 128 129 130 131 132 133 134 140 141 142 143	3 4 6 7 15 16 18 24 26 30 33 34 36 40 42 51 52 53 54 55 56 57 58 80 81 82 87 88 89 92 93 95 96 97 100 101 102 103 104 105 106 107 144 145 146 147 148 149 150	8 9 10 12 14 19 20 23 27 28 31 37 38 41 43 47 48 62 63 64 65 66 67 68 69 70 83 84 85 91 94 108 109 110 111 112 113 114 115 116 117 118 119 120 135 136 137 138 139
Final Cluster		
Cluster1	Cluster2	Cluster3
1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28 29 30 31 32 33 34 35 36 37 38 39 40 41 42 43 44 45 46 47 48 49 50	51 52 53 54 55 56 57 58 59 60 61 62 63 64 65 66 67 68 69 70 71 72 73 74 75 76 77 78 79 80 81 82 83 84 85 86 87 88 89 90 91 92 93 94 95 96 97 98 99 100 101 102 103 104 105 107	106 108 109 110 111 112 113 114 115 116 117 118 119 120 121 122 123 124 125 126 127 128 129 130 131 132 133 134 135 136 137 138 139 140 141 142 143 144 145 146 147 148 149 150
Count error=6		
Accuracy = = 96 %		

Table 5.6: Result of GA-R2 using Iris Data

	Iris-setosa	**Iris-versicolor**	**Iris-virginica**	**Total**
The right number of data point	50	50	50	150
Details of Data points wrongly clustered	NIL	NIL	101 102 103 104 105 107	101 102 103 104 105 107
number of data point wrongly clustered	0	0	6	6
The number of data point correctly clustered	50	50	44	144
Accuracy (%)	100	100	88	96

Table 5.7: Initial and final cluster distribution for GA-R3 for Iris Data.

Initial cluster		
Cluster1	Cluster2	Cluster3
11 12 13 14 15 16 17 18 19 20 21 22 24 27 30 32 33 34 35 39 43 44 45 46 47 48 59 60 61 62 63 64 65 66 67 68 69 70 129 130 131 132 133 134 135 136 137 138 139	1 2 3 4 5 6 7 8 9 10 23 25 26 28 29 31 36 37 38 40 41 42 49 50 51 52 53 54 55 56 57 58 108 109 110 111 112 113 114 115 116 117 118 119 120 144 145 146 147 148 149 150	71 72 73 74 75 76 77 78 79 80 81 82 83 84 85 86 87 88 89 90 91 92 93 94 95 96 97 98 99 100 101 102 103 104 105 106 107 121 122 123 124 125 126 127 128 140 141 142 143
Final Cluster		
Cluster 1	Cluster 2	Cluster 3
101 102 103 104 105 106 107 108 109 110 111 112 113 114 115 116 117 118 119 120 121 122 123 124 125 126 127 128 129 130 131 132 133 134 135 136 137 138 139 140 141 142 143 144 145 146 147 148 149 150	1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28 29 30 31 32 33 34 35 36 37 38 39 40 41 42 43 44 45 46 47 48 49 50	51 52 53 54 55 56 57 58 59 60 61 62 63 64 65 66 67 68 69 70 71 72 73 74 75 76 77 78 79 80 81 82 83 84 85 86 87 88 89 90 91 92 93 94 95 96 97 98 99 100
Count error= 0		
Accuracy = 100 %		

Table 5.8: Analysis of Best case, Average case, worst case for GA using Iris

Representation R1			
	Best case	Average Case	Worst case
Count error Accuracy (%)	10 93.33	12 92	14 90.67
Representation R2			
	Best case	Average Case	Worst case
Count error Accuracy (%)	6 96	6 96	6 96
Representation R3			
	Best case	Average Case	Worst case
Count error Accuracy (%)	0 100	8 94.67	23 84.67

Table 5.9 summarizes the result of GA clustering algorithm for WBCD. It can be easily infer from Table 5.9 that GA-based clustering algorithm performs better compared to Non-GA based clustering algorithm for WBCD.

Table 5.10 shows the result obtained by GA-R1 based clustering algorithm for WBCD. Table 5.11 shows the result obtained by GA-R2 based clustering algorithm for WBCD. Table 5.12 shows the result obtained by GA-R3 based clustering algorithm for WBCD. It may be noted that previous work related to WBCD in literature deals only with classification accuracy [140], [127]. Taking SCM into account, it can be say that any clustering algorithm which gives count error less than 70 (i.e. accuracy of approx 90%) can be treated as good clustering algorithm.

GA-R1 achieves accuracy upto 96.1933% and count error as 26 in case of WBCD. Data point { 446 448 576 577 578 579 580 581 582 583 584 585 586 587 588 589 590 591

592 593 594 600} which are Benign, are wrongly clustered into Malignant, whereas data points {2 4 139 244} are malignant in nature, but are wrongly clustered into Benign.

GA-R2 achieves accuracy upto 96.7789% and count error in this case obtained to be 37. Data point { 2 4 139 244} which are Benign, are wrongly clustered into Malignant whereas data points {446 448 576 577 578 579 580 581 582 583 584 585 586 587 588 589 590 591 592 593 594} which are malignant in nature are wrongly clustered into Benign.

Final fitness value of GA based clustering algorithm for five run has been tabulated in Table 5.13 and Table 5.14 for Iris and WBCD respectively.

Table 5.15 consists of the optimal fitness value for Iris and WBCD data for GA-R1, GA-R2 and GA-R3 based clustering algorithms.

Table 5.9: Comparison of clustering algorithm for WBCD

Algorithm	Count Error	Percentage error	Percentage Accuracy
HCM	29	4.2460	95.7540
SCM	27	3.9531	96.0469
GA(Representation 1)	26	657	96.1933
GA(Representation 2)	22	661	96.7789
GA(Representation 3)	18	665;	97.3646

Table 5.10: Result of GA-R1 using WBCD

	Benign	Malignant	Total
The right number of data point	444	239	683
Details of Data points wrongly clustered	2 4 139 244	446 448 576 577 578 579 580 581 582 583 584 585 586 587 588 589 590 591 592 593 594 600	2 4 139 244 446 448 576 577 578 579 580 581 582 583 584 585 586 587 588 589 590 591 592 593 594 600
number of data point wrongly clustered	4	22	26
The number of data point correctly clustered	441	217	657
Accuracy (%)	99.324	90. 8	98.83

Table 5.11: Result of GA-R2 using WBCD

	Benign	Malignant	Total
The right number of data point	444	239	683
Details of Data points wrongly clustered	NIL	446 448 576 577 578 579 580 581 582 583 584 585 586 587 588 589 590 591 592 593 594 600	446 448 576 577 578 579 580 581 582 583 584 585 586 587 588 589 590 591 592 593 594 600
number of data point wrongly clustered	0	22	22
The number of data point correctly clustered	444	217	661
Accuracy (%)	100	88.93	96.78

Table 5.12: Result of GA-R3 using WBCD

	Benign	Malignant	Total
The right number of data point	444	239	683
Details of Data points wrongly clustered	NIL	446 448 580 581 582 583 584 585 586 587 588 589 590 591 592 593 594 600	446 448 580 581 582 583 584 585 586 587 588 589 590 591 592 593 594 600
number of data point wrongly clustered	0	18	18
The number of data point correctly clustered	444	221	665
Accuracy (%)	100	92.5	97.36

Table 5.13: Fitness Function values for different Run for Iris data.

Trial No.	Iris Data		
	GA-R1	**GA-R2**	**GA-R3**
1	0.0099	0.0109	0.0103
2	0.0099	0.0109	0.0103
3	0.0097	0.0109	0.0099
4	0.0099	0.0103	0.0101
5	0.0099	0.0109	0.0103

Table 5.14: Fitness Function values for different Run for WBCD data.

Trial No.	WBCD Data		
	GA-R1	**GA-R2**	**GA-R3**
1	0.00171	0.00173	0.00170
2	0.00171	0.00173	0.00170
3	0.00167	0.00173	0.00158
4	0.00167	0.00173	0.00158
5	0.00158	0.00173	0.00158

Table 5.15: Final Fitness Function value for machine learning Data

Dataset Sl. No.	**Datasets**	GA-R1	GA-R2	GA-R3
1	**Iris**	0.0097	0.0103	0.0101
2	**WBCD**	0.00158	0.00173	0.00158

5.3.3 Experiment 2: Bioinformatics Data

In this section, discussion has been made on Family of GA based Clustering algorithm to all the bioinformatics data stated in section 4.1.1. Thirteen microarray data has been considered for simulation studies. These data are: Iyer data/Serum data, Cho data (yeast data), Leukemia (Golub Experiment), Breast data A, Breast data B, Breast Multi data A, Breast Multi data B, DLBCL A, DLBCL B, DLBCL C, DLBCL D, Lung Cancer, St. Jude Leukemia data. The details of these data has been already explained in section 4.1.1. Complete result of GA Clustering result for each individual bioinformatics data is given in appendix F.

5.3.4 Results and Discussion

The parameters used for GA based clustering algorithm for Bioinformatics data is shown in Table 5.16

Table 5.17 to Table 5.29 shows the result obtained by GA-R1 for bioinformatics data. All these data contains the following information of GA-R1 for bioinformatics data:

the right number of data point in each cluster, details of data points wrongly clustered in each cluster, number of data points in each cluster, number of data point correctly clustered in each cluster and individual accuracy of each cluster of a data as well as overall accuracy for each bioinformatics data.

Table 5.17 contains the result obtained by GA-R1 for Breast Data A. Number of data point wrongly clustered in cluster 1 is one, in cluster 2 is six and in cluster 3 is three. The total number of data points wrongly clustered is ten. Details of the data point wrongly clustered are {11 20 31 38 39 46 56 66 80 81}. The overall accuracy obtained for Breast Data A using GA-R1 was 89.8 % .

Table 5.18 contains the result obtained by GA-R1 for Breast Data B. Details of the data point wrongly clustered are {31 35 36 41 42 43 44 47 48 49}. It may be noted that cluster 1 and cluster 2 achieves 100 % accuracy . The overall accuracy obtained for Breast Data B using GA-R1 was 77.57 % .

Table 5.19 contains the result obtained by GA-R1 for Breast Multi Data A. Details of the data point wrongly clustered are {2 15 19}. Notably cluster 2, cluster 3 and cluster 4 achieves accuracy of 100 %. The overall accuracy obtained for Breast Multi Data A using GA-R1 was 97.08 % .

Table 5.20 contains the result obtained by GA-R1 for Breast Multi Data B. The total number of data points wrongly clustered is twelve. The overall accuracy obtained for Breast Multi Data B using GA-R1 was 62.5 % .

Table 5.21 contains the result obtained by GA-R1 for DLBCL A. The total number of data points wrongly clustered is 43. The overall accuracy obtained for DLBCL A using GA-R1 was 69.5 %.

Table 5.22 contains the result obtained by GA-R1 for DLBCL B. The total number of data points wrongly clustered is 28. The overall accuracy obtained for DLBCL B using GA-R1 was 84.45 % .

Table 5.23 contains the result obtained by GA-R1 for DLBCL C. The total number of data points wrongly clustered is 12. Note that cluster 2 achieves 100% accuracy. The overall accuracy obtained for DLBCL C using GA-R1 was 84.45 %.

Table 5.24 contains the result obtained by GA-R1 for DLBCL D The total number of data points wrongly clustered is 44. The overall accuracy obtained for DLBCL D using GA-R1 was 65.89 %.

Table 5.25 contains the result obtained by GA-R1 for Lung Cancer. The total number of data points wrongly clustered is 42. The overall accuracy obtained for Lung Cancer using GA-R1 was 78.68%.

Table 5.26 contains the result obtained by GA-R1 for Leukemia Cancer. The total number of data points wrongly clustered is 32. The overall accuracy obtained for Leukemia Cancer using GA-R1 was 55.56%.

Table 5.27 contains the result obtained by GA-R1 for St. Jude Leukemia Cancer. The total number of data points wrongly clustered is 15. Notably cluster 2 and cluster 6 achieves accuracy 100%. The overall accuracy obtained for St. jude Leukemia Cancer using GA-R1 was 93.95 %.

Table 5.28 contains the result obtained by GA-R1 for Cho data. The total number of data points wrongly clustered is 127. The overall accuracy obtained for Cho data using GA-R1 was 67.1 %.

Table 5.29 contains the result obtained by GA-R1 for Iyer data. The total number of data points wrongly clustered is 248. The overall accuracy obtained for Iyer data using GA-R1 was 52.03 %.

Table 5.16: Parameter used in GA based clustering Algorithm for Bioinformatics data

Parameter	Value
Population Size	20 - 150
Maximum No. Of Iteration	10 - 50
Crossover Probability	0.6 - 0.8
Mutation Probability	0.001 - 0.01

Table 5.17: Result of Breast data A (GA-R1)

Breast data A				
	Cluster 1	Cluster 2	Cluster 3	Total
The right number of data point	11	51	36	98
Details of Data points wrongly clustered	11	20 31 38 39 46 56	66 80 81	11 20 31 38 39 46 56 66 80 81
number of data point wrongly clustered	1	6	3	10
The number of data point correctly clustered	10	45	33	88
Accuracy (%)	90.91	88.26	91.67	89.8

Table 5.18: Result of Breast data B (GA-R1)

Breast data B					
	Cluster 1	Cluster 2	Cluster 3	Cluster 4	Total
The right number of data point	12	11	7	19	49
Details of Data points wrongly clustered	NIL	NIL	29	31 35 36 41 42 43 44 47 48 49	31 35 36 41 42 43 44 47 48 49
number of data point wrongly clustered	0	0	1	10	11
The number of data point correctly clustered	12	11	6	9	38
Accuracy (%)	100	100	85.71	47.37	77.57

Table 5.19: Result of Breast Multi data A (GA-R1)

Multi Breast data A					
	Cluster 1	Cluster 2	Cluster 3	Cluster 4	Total
The right number of data point	26	26	28	23	103
Details of Data points wrongly clustered	2 15 19	NIL	NIL	NIL	2 15 19
number of data point wrongly clustered	3	0	0	0	3
The number of data point correctly clustered	23	26	28	23	100
Accuracy (%)	88.46	100	100	100	97.08

Table 5.20: Result of Breast Multi Data B (GA-R1)

Multi Breast data B					
	Cluster 1	Cluster 2	Cluster 3	Cluster 4	Total
The right number of data point	5	9	7	11	32
Details of Data points wrongly clustered	1 4 5	12 13	15 16 19	23 28 29 30	1 4 5 12 13 15 16 19 23 28 29 30
number of data point wrongly clustered	3	2	3	4	12
The number of data point correctly clustered	2	7	4	7	20
Accuracy (%)	40	77.78	57.14	63.63	62.5

Table 5.21: Result of DLBCL A (GA-R1)

DLBCL A				
	Cluster 1	Cluster 2	Cluster 3	Total
The right number of data point	49	50	42	141
Details of Data points wrongly clustered	3 4 9 15 16 21 22 24 29 43 44 45 46 48	51 59 61 62 65 67 70 76 78 92 93 95 97 98	109 113 115 118 120 128 130 133 134 135 136 137 138 140 141	3 4 9 15 16 21 22 24 29 43 44 45 46 48 51 59 61 62 65 67 70 76 78 92 93 95 97 98 109 113 115 118 120 128 130 133 134 135 136 137 138 140 141
number of data point wrongly clustered	14	14	15	43
The number of data point correctly clustered	35	36	27	98
Accuracy (%)	71.43	72	64.3	69.5

Table 5.22: Result of DLBCL B (GA-R1)

DLBCL B				
	Cluster 1	Cluster 2	Cluster 3	Total
The right number of data point	42	51	87	180
Details of Data points wrongly clustered	2 14 15 16 32 34 35 36 37 39 40 41	46 47 49 51 58 65 92	97 103 119 121 122 124 164 167 179	2 14 15 16 32 34 35 36 37 39 40 41 46 47 49 51 58 65 92 97 103 119 121 122 124 164 167 179
number of data point wrongly clustered	12	7	9	28
The number of data point correctly clustered	30	44	78	152
Accuracy (%)	71.43	86.27	89.66	84.45

Table 5.23: Result of DLBCL C (GA-R1)

DLBCL C					
	Cluster 1	Cluster 2	Cluster 3	Cluster 4	Total
The right number of data point	17	16	13	12	58
Details of Data points wrongly clustered	12	NIL	35 38 40 41 42 43 45	52 53 57 58	12 35 38 40 41 42 43 45 52 53 57 58
number of data point wrongly clustered	1	0	7	4	12
The number of data point correctly clustered	5	16	6	8	35
Accuracy (%)	29.41	100	46.15	66.67	60.35

Table 5.24: Result of DLBCL D (GA-R1)

DLBCL D					
	Cluster 1	Cluster 2	Cluster 3	Cluster 4	Total
The right number of data point	19	37	24	49	129
Details of Data points wrongly clustered	1 7 9 13 17 19	20 28 30 32 40 41 42 43 45 48 51 56	63	81 82 83 84 85 86 87 88 89 90 91 92 93 94 95 96 97 98 100 104 105 108 112 114 117	1 7 9 13 17 19 20 28 30 32 40 41 42 43 45 48 51 56 63 81 82 83 84 85 86 87 88 89 90 91 92 93 94 95 96 97 98 100 104 105 108 112 114 117
number of data point wrongly clustered	6	12	1	25	44
The number of data point correctly clustered	13	25	23	24	85
Accuracy (%)	68.42	67.57	95.83	48.98	65.89

Table 5.25: Result of Lung Cancer (GA-R1)

Lung Cancer					
	Cluster 1	Cluster 2	Cluster 3	Cluster4	Total
The right number of data point	139	17	21	20	197
Details of Data points wrongly clustered	15 18 19 20 21 24 26 33 42 50 68 69 71 76 78 79 86 89 90 92 93 97 104 105 109 111 112 114 117 126 135 137 139	144	157 162 167 168 169 174	196	15 18 19 20 21 24 26 33 42 50 68 69 71 76 78 79 86 89 90 92 93 97 104 105 109 111 112 114 117 126 135 137 139 144 157 162 167 168 169 174 196
number of data point wrongly clustered	34	1	6	1	42
The number of data point correctly clustered	105	16	15	19	155
Accuracy (%)	75.54	94.12	71.43	95	78.68

Table 5.26: Result of Leukemia (GA-R1)

Leukemia			
	Cluster 1	Cluster 2	Total
The right number of data point	47	25	72
Details of Data points wrongly clustered	6 7 8 22 23 28 31 32 33 34 35 36 39 40 41 42 45	48 50 51 52 53 54 55 56 57 58 59 61 62 69 71	6 7 8 22 23 28 31 32 33 34 35 36 39 40 41 42 45 48 50 51 52 53 54 55 56 57 58 59 61 62 69 71
number of data point wrongly clustered	17	15	32
The number of data point correctly clustered	30	10	40
Accuracy (%)	63.83	40	55.56

Table 5.27: Result of St. Jude Leukemia (GA-R1)

St. Jude Leukemia							
	Cluster 1	Cluster 2	Cluster 3	Cluster4	Cluster5	Cluster6	Total
The right number of data point	15	27	64	20	43	79	248
Details of Data points wrongly clustered	2	NIL	61 69 71 99	109 110 111 112	131 133 143 144 157 168	NIL	2 61 69 71 99 109 110 111 112 131 133 143 144 157 168
number of data point wrongly clustered	1	0	4	4	6	0	15
The number of data point correctly clustered	14	27	60	16	37	79	233
Accuracy (%)	93.33	100	93.75	80	86.04	100	93.95

Table 5.28: Result of Cho Data (GA-R1)

Cho Data						
	Cluster 1	Cluster 2	Cluster 3	Cluster 4	Cluster 5	Total
The right number of data point	67	135	75	54	55	386
Details of Data points wrongly clustered	2 6 25 26 28 32 43 45 56 64 65 66	79 82 86 89 90 96 97 100 101 105 110 112 115 119 125 127 128 129 130 131 132 133 134 136 137 138 143 144 145 146 147 162 168 173 174 176 178 180 181 183 184 185 186 187 188 189 190 191 194 196 198 199 200 201 202	215 217 218 220 221 222 225 226 227 228 229 231 236 237 238 239 241 243 246 247 248 249 250 251 254 255 256 257 258 259 268 269 270 272 273 276 277	280 283 284 291 293 294 296 297 299 313 319 320 321 322 324	332 342 347 354 359 361 366 370	2 6 25 26 28 32 43 45 56 64 65 66 79 82 86 89 90 96 97 100 101 105 110 112 115 119 125 127 128 129 130 131 132 133 134 136 137 138 143 144 145 146 147 162 168 173 174 176 178 180 181 183 184 185 186 187 188 189 190 191 194 196 198 199 200 201 202 215 217 218 220 221 222 225 226 227 228 229 231 236 237 238 239 241 243 246 247 248 249 250 251 254 255 256 257 258 259 268 269 270 272 273 276 277 280 283 284 291 293 294 296 297 299 313 319 320 321 322 324 332 342 347 354 359 361 366 370
number of data point wrongly clustered	12	55	37	15	8	127
The number of data point correctly clustered	55	80	38	39	47	259
Accuracy (%)	82.1	59.26	50.67	72.22	85.45	67.1

Table 5.29: Iyer Data(GA-R1)

Iyer Data					
	The right number of data point	Details of Data points wrongly clustered	Number of data point wrongly clustered	The number of data point correctly clustered	Accuracy (%)
Cluster1	33	1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 21 22 23 28 29 30 31	26	7	78.79
Cluster2	100	NIL	0	100	100
Cluster3	145	143 146 157 161 162 163 164 166 167 168 169 170 171 172 173 174 175 176 177 178 179 180 181 186 187 188 190 191 192 193 194 197 198 199 200 201 202 203 204 206 210 211 213 224 225 226 231 243 244 245 248 249 255 265 267 270 271 273 274 275 278	61	84	57.93
Cluster4	34	280 283 284 285 286 287 294 295 296 297 298 299 300 301 303	15	19	55.88
Cluster5	43	313 314 315 316 317 318 319 320 321 322 324 325 326 327 328 329 330 331 332 333 334 335 342 343 348 349 352 355	28	15	34.89
Cluster6	7	359	1	6	85.71
Cluster7	34	365 366 367 370 373 378 379 381 383 384 387 388 389 390 391 392 393	17	17	50
Cluster8	14	399 401	2	12	85.71
Cluster9	63	411 412 413 414 415 416 417 418 419 420 421 422 423 424 426 427 428 429 430 431 432 433 434 436 437 438 439 440 442 443 444 445 447 448 449 450 451 452 453 454 455 456 457 458 459 460 461 462 463 464 465 466 467 468 469 473	56	7	11.11
Cluster10	19	474 475 476 477 478 479 480 481 482 483 484 485 486 487 488 489 490 492	18	1	5.26
Cluster11	25	493 494 495 496 497 498 499 500 502 503 504 505 506 507 508 509 510 511 512 513 514 515 516 517	24	1	4
Total	517	1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 21 22 23 28 29 30 31 143 146 157 161 162 163 164 166 167 168 169 170 171 172 173 174 175 176 177 178 179 180 181 186 187 188 190 191 192 193 194 197 198 199 200 201 202 203 204 206 210 211 213 224 225 226 231 243 244 245 248 249 255 265 267 270 271 273 274 275 278 280 283 284 285 286 287 294 295 296 297 298 299 300 301 303 313 314 315 316 317 318 319 320 321 322 324 325 326 327 328 329 330 331 332 333 334 335 342 343 348 349 352 355 359 365 366 367 370 373 378 379 381 383 384 387 388 389 390 391 392 393 399 401 411 412 413 414 415 416 417 418 419 420 421 422 423 424 426 427 428 429 430 431 432 433 434 436 437 438 439 440 442 443 444 445 447 448 449 450 451 452 453 454 455 456 457 458 459 460 461 462 463 464 465 466 467 468 469 473 474 475 476 477 478 479 480 481 482 483 484 485 486 487 488 489 490 492 493 494 495 496 497 498 499 500 502 503 504 505 506 507 508 509 510 511 512 513 514 515 516 517	248	269	52.03

Table 5.30 to Table 5.42 shows the result obtained by GA-R2 for bioinformatics data. All these table contains the following information of GA-R2 for bioinformatics data: the right number of data point in each cluster, details of data points wrongly clustered in each cluster, number of data points in each cluster, number of data point correctly clustered in each cluster and individual accuracy of each cluster as well as overall accuracy for each bioinformatics data.

Table 5.30 contains the result obtained by GA-R2 for Breast Data A. Number of data point wrongly clustered in cluster 1 is one, in cluster 2 is five and in cluster 3 is one. The total number of data points wrongly clustered is seven. Details of the data points wrongly clustered are {11 20 31 38 39 46 56 66 80 }. The overall accuracy obtained for Breast Data A using GA-R2 was 92.86 % .

Table 5.31 contains the result obtained by GA-R2 for Breast Data B. Details of the data point wrongly clustered are {29 31 35 36 41 42 43 44 47 48 49 }. Notably cluster 1 and cluster 2 achieves accuracy of 100 %. The overall accuracy obtained for Breast Data B using GA-R2 was 77.55% .

Table 5.32 contains the result obtained by GA-R1 for Breast Multi Data A. Details of the data point wrongly clustered are {2 15 19}. Notably cluster 2, cluster 3 and cluster 4 achieves accuracy 100 %. The overall accuracy obtained for Breast Multi Data A using GA-R2 was 97.09 % .

Table 5.33 contains the result obtained by GA-R2 for Breast Multi Data B. The total number of data points wrongly clustered is nine. The overall accuracy obtained for Breast Multi Data B using GA-R2 was 71.88 % .

Table 5.34 contains the result obtained by GA-R2 for DLBCL A. The total number of data points wrongly clustered is 49. The overall accuracy obtained for DLBCL A using GA-R2 was 65.3 %.

Table 5.35 contains the result obtained by GA-R2 for DLBCL B. The total number of data points wrongly clustered is 33. The overall accuracy obtained for DLBCL B using GA-R2 was 81.67 % .

Table 5.36 contains the result obtained by GA-R2 for DLBCL C. The total number of data points wrongly clustered is 18. Note that cluster 2 achieves 100% accuracy. The overall accuracy obtained for DLBCL C using GA-R2 was 68.97 % .

Table 5.37 contains the result obtained by GA-R2 for DLBCL D The total number of data points wrongly clustered is 36. The overall accuracy obtained for DLBCL D using GA-R2 was 72.09 %.

Table 5.38 contains the result obtained by GA-R2 for Lung Cancer. The total number of data points wrongly clustered is 32. The overall accuracy obtained for Lung Cancer using GA-R2 was 83.76 %.

Table 5.39 contains the result obtained by GA-R2 for Leukemia Cancer. The total number of data points wrongly clustered is 22. The overall accuracy obtained for Leukemia Cancer using GA-R2 was 69.44%.

Table 5.40 contains the result obtained by GA-R2 for St. Jude Leukemia Cancer. The total number of data points wrongly clustered is 13. Notably cluster 2 and cluster 6 achieves accuracy 100%. The overall accuracy obtained for St. jude Leukemia Cancer using GA-R2 was 94.35 %.

Table 5.41 contains the result obtained by GA-R2 for Cho data. The total number of data points wrongly clustered is 99. The overall accuracy obtained for Cho data using GA-R2 was 74.35 %.

Table 5.42 contains the result obtained by GA-R2 for Iyer data. The total number of data points wrongly clustered is 251. The overall accuracy obtained for Iyer data using GA-R2 was 51.45%.

Table 5.30: Breast data A(GA-R2)

Breast data A				
	Cluster 1	Cluster 2	Cluster 3	Total
The right number of data point	11	51	36	98
Details of Data points wrongly clustered	11	20 31 38 46 56	80	11 20 31 38 46 56 80
number of data point wrongly clustered	1	5	1	7
The number of data point correctly clustered	10	46	35	91
Accuracy (%)	90.91	90.2	97.22	92.86

Table 5.31: Result of Breast data B (GA-R2)

Breast data B					
	Cluster 1	Cluster 2	Cluster 3	Cluster 4	Total
The right number of data point	12	11	7	19	49
Details of Data points wrongly clustered	NIL	NIL	29	31 35 36 41 42 43 44 47 48 49	29 31 35 36 41 42 43 44 47 48 49
number of data point wrongly clustered	0	0	1	10	11
The number of data point correctly clustered	12	11	6	9	38
Accuracy (%)	100	100	85.71	47.37	77.55

Table 5.32: Result of Breast Multi data A (GA-R2)

Breast Multi data A					
	Cluster 1	Cluster 2	Cluster 3	Cluster 4	Total
The right number of data point	26	26	28	23	103
Details of Data points wrongly clustered	2 15 19	NIL	NIL	NIL	2 15 19
number of data point wrongly clustered	3	0	0	0	3
The number of data point correctly clustered	23	26	28	23	100
Accuracy (%)	88.46	100	100	100	97.09

Table 5.33: Result of Breast Multi data B (GA-R2)

Breast Multi data B					
	Cluster 1	Cluster 2	Cluster 3	Cluster 4	Total
The right number of data point	5	9	7	11	32
Details of Data points wrongly clustered	1 4 5	12 13	15 16 19	30	1 4 5 12 13 15 16 19 30
number of data point wrongly clustered	3	2	3	1	9
The number of data point correctly clustered	2	7	4	10	23
Accuracy (%)	40	77.78	57.14	90.91	71.88

Table 5.34: Result of DLBCL A (GA-R2)

DLBCL A				
	Cluster 1	Cluster 2	Cluster 3	Total
The right number of data point	49	50	42	141
Details of Data points wrongly clustered	3 4 9 15 16 21 22 23 24 26 29 43 44 45 46 48	51 52 56 59 61 62 65 67 68 70 76 78 85 92 93 95 97 98	109 113 115 118 120 128 130 133 134 135 136 137 138 140 141	3 4 9 15 16 21 22 23 24 26 29 43 44 45 46 48 51 52 56 59 61 62 65 67 68 70 76 78 85 92 93 95 97 98 109 113 115 118 120 128 130 133 134 135 136 137 138 140 141
number of data point wrongly clustered	16	18	15	49
The number of data point correctly clustered	33	32	27	92
Accuracy (%)	67.35	64	64.3	65.3

Table 5.35: Result of DLBCL B (GA-R2)

DLBCL B				
	Cluster 1	Cluster 2	Cluster 3	Total
The right number of data point	42	51	87	180
Details of Data points wrongly clustered	2 3 5 14 15 16 32 34 35 36 37 39 40 41	46 47 49 51 58 65 77 79 92	96 97 103 119 121 122 124 164 167 179	2 3 5 14 15 16 32 34 35 36 37 39 40 41 46 47 49 51 58 65 77 79 92 96 97 103 119 121 122 124 164 167 179
number of data point wrongly clustered	14	9	10	33
The number of data point correctly clustered	28	42	77	147
Accuracy (%)	66.67	82.35	88.51	81.67

Table 5.36: Result of DLBCL C (GA-R2)

DLBCL C					
	Cluster 1	Cluster 2	Cluster 3	Cluster 4	Total
The right number of data point	17	16	13	12	58
Details of Data points wrongly clustered	1 9 12	NIL	35 38 40 41 42 43 45	48 52 53 54 55 56 57 58	1 9 12 35 38 40 41 42 43 45 48 52 53 54 55 56 57 58
number of data point wrongly clustered	3	0	7	8	18
The number of data point correctly clustered	14	16	6	4	40
Accuracy (%)	82.35	100	46.15	33.33	68.97

Table 5.37: Result of DLBCL D (GA-R2)

DLBCL D					
	Cluster 1	Cluster 2	Cluster 3	Cluster4	Total
The right number of data point	19	37	24	49	129
Details of Data points wrongly clustered	1 17	20 28 32 43 45 48 51 56	63	81 82 83 84 85 86 87 88 89 90 91 92 93 94 95 96 97 98 100 104 105 108 112 114 117	1 17 20 28 32 43 45 48 51 56 63 81 82 83 84 85 86 87 88 89 90 91 92 93 94 95 96 97 98 100 104 105 108 112 114 117
number of data point wrongly clustered	2	8	1	25	36
The number of data point correctly clustered	17	29	23	24	93
Accuracy (%)	89.47	78.38	95.83	48.98	72.09

Table 5.38: Result of Lung Cancer (GA-R2)

Lung Cancer					
	Cluster 1	Cluster 2	Cluster 3	Cluster4	Total
The right number of data point	139	17	21	20	197
Details of Data points wrongly clustered	15 24 26 68 71 78 79 86 89 90 92 93 97 104 105 109 111 112 114 117 126 135 137 139	144	157 162 167 168 169 174	196	15 24 26 68 71 78 79 86 89 90 92 93 97 104 105 109 111 112 114 117 126 135 137 139 144 157 162 167 168 169 174 196
number of data point wrongly clustered	24	1	6	1	32
The number of data point correctly clustered	115	16	15	19	165
Accuracy (%)	82.73	94.12	71.43	95	83.76

Table 5.39: Result of Leukemia (GA-R2)

Leukemia			
	Cluster 1	Cluster 2	Total
The right number of data point	47	25	72
Details of Data points wrongly clustered	6 7 8 22 23 28 31 32 33 34 35 36 39 40 41 42 45	48 52 53 54 69	6 7 8 22 23 28 31 32 33 34 35 36 39 40 41 42 45 48 52 53 54 69
number of data point wrongly clustered	17	5	22
The number of data point correctly clustered	30	20	50
Accuracy (%)	63.83	80	69.44

Table 5.40: Result of St. Jude Leukemia (GA-R2)

St. Jude Leukemia							
	Cluster 1	Cluster 2	Cluster 3	Cluster 4	Cluster 5	Cluster 6	Total
The right number of data point	15	27	64	20	43	79	248
Details of Data points wrongly clustered	2	NIL	61 69 71 99	109 110 111 112	131 144 157 168	NIL	2 61 69 71 99 109 110 111 112 131 144 157 168
number of data point wrongly clustered	1	0	4	4	4	0	13
The number of data point correctly clustered	13	27	60	16	39	79	234
Accuracy (%)	86.67	100	93.75	80	90.7	100	94.35

Table 5.41: Result of Cho Data (GA-R2)

Cho Data						
	Cluster 1	Cluster 2	Cluster 3	Cluster4	Cluster5	Total
The right number of data point	67	135	75	54	55	386
Details of Data points wrongly clustered	2 6 25 26 28 32 43 45 56 64 66	82 90 96 110 112 125 127 128 129 130 133 134 137 146 173 176 178 180 181 187 188 189 190 191 199	203 205 207 210 212 215 217 218 220 221 222 225 226 227 228 229 231 236 237 238 239 241 243 246 247 248 249 250 251 254 255 256 257 258 259 260 261 262 263 268 269 270 272 273 276 277	291 293 294 296 297 299 321 322 324	332 342 347 354 359 361 366 370	2 6 25 26 28 32 43 45 56 64 66 82 90 96 110 112 125 127 128 129 130 133 134 137 146 173 176 178 180 181 187 188 189 190 191 199 203 205 207 210 212 215 217 218 220 221 222 225 226 227 228 229 231 236 237 238 239 241 243 246 247 248 249 250 251 254 255 256 257 258 259 260 261 262 263 268 269 270 272 273 276 277 291 293 294 296 297 299 321 322 324 332 342 347 354 359 361 366 370
number of data point wrongly clustered	11	25	46	9	8	99
The number of data point correctly clustered	56	110	29	45	47	287
Accuracy (%)	83.58	81.48	38.67	83.33	85.45	74.35

Table 5.42: Result of Iyer Data (GA-R2)

Iyer Data	The right number of data point	Details of Data points wrongly clustered	number of data point wrongly clustered	The number of data point correctly clustered	Accuracy (%)
Cluster 1	33	1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 21 22 23 28 29 30 31	26	7	21.21
Cluster 2	100	NIL	0	100	100
Cluster 3	145	143 146 157 161 162 163 164 166 167 168 169 170 171 172 173 174 175 176 177 178 179 180 181 186 187 188 190 191 192 193 194 197 198 199 200 201 202 203 204 206 210 211 213 224 225 226 231 243 244 245 248 249 255 265 267 270 271 273 274 275 278	61	84	57.93
Cluster 4	34	280 283 284 285 286 287 294 295 296 297 298 299 300 301 303	15	19	55.82
Cluster 5	43	313 314 315 316 317 318 319 320 321 322 324 325 326 327 328 329 330 331 332 333 334 335 342 343 348 349 352 355	28	15	34.89
Cluster 6	7	359	1	6	85.71
Cluster 7	34	365 366 367 370 373 378 379 381 383 384 387 388 389 390 391 392 393	17	17	50
Cluster 8	14	399 401	2	12	85.71
Cluster 9	63	411 412 413 414 415 416 417 418 419 420 421 422 423 424 425 426 427 428 429 430 431 432 433 434 436 437 438 439 440 442 443 444 445 446 447 448 449 450 451 452 453 454 455 456 457 458 459 460 461 462 463 464 465 466 467 468 469 470 473	59	4	6.35
Cluster 10	19	474 475 476 477 478 479 480 481 482 483 484 485 486 487 488 489 490 492	18	1	5.26
Cluster 11	25	493 494 495 496 497 498 499 500 502 503 504 505 506 507 508 509 510 511 512 513 514 515 516 517	24	1	4
Total	517	1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 21 22 23 28 29 30 31 143 146 157 161 162 163 164 166 167 168 169 170 171 172 173 174 175 176 177 178 179 180 181 186 187 188 190 191 192 193 194 197 198 199 200 201 202 203 204 206 210 211 213 224 225 226 231 243 244 245 248 249 255 265 267 270 271 273 274 275 278 280 283 284 285 286 287 294 295 296 297 298 299 300 301 303 313 314 315 316 317 318 319 320 321 322 324 325 326 327 328 329 330 331 332 333 334 335 342 343 348 349 352 355 359 365 366 367 370 373 378 379 381 383 384 387 388 389 390 391 392 393 399 401 411 412 413 414 415 416 417 418 419 420 421 422 423 424 425 426 427 428 429 430 431 432 433 434 436 437 438 439 440 442 443 444 445 446 447 448 449 450 451 452 453 454 455 456 457 458 459 460 461 462 463 464 465 466 467 468 469 470 473 474 475 476 477 478 479 480 481 482 483 484 485 486 487 488 489 490 492 493 494 495 496 497 498 499 500 502 503 504 505 506 507 508 509 510 511 512 513 514 515 516 517	251	266	51.45

Table 5.43 to Table 5.55 shows the result obtained by GA-R3 for bioinformatics data. All these table contains the following information of GA-R3 for bioinformatics data: The right number of data point in each cluster, details of data point wrongly clustered in each cluster, number of data points in each cluster, number of data point correctly clustered in each cluster and individual accuracy of each cluster in a data as well as overall accuracy for each bioinformatics data.

Table 5.43 contains the result obtained by GA-R3 for Breast Data A. Number of data point wrongly clustered in cluster 1 is five, in cluster 2 is six and in cluster 3 is three. The total number of data points wrongly clustered is 14. Details of the data point wrongly clustered are {5 6 7 8 11 20 31 38 39 46 56 66 80 81}. The overall accuracy obtained for Breast Data A using GA-R3 was 85.71 % .

Table 5.44 contains the result obtained by GA-R3 for Breast Data B. Details of the data point wrongly clustered are {17 28 31 35 36 41 42 47 48 49}. Notably cluster 1 achieves accuracy 100 %. The overall accuracy obtained for Breast Data B using GA-R3 was 79.59 % .

Table 5.45 contains the result obtained by GA-R3 for Breast Multi Data A. Details of the data point wrongly clustered are {2 15 19 25 26 38 60 70}. The overall accuracy obtained for Breast Multi Data A using GA-R3 was 92.23 % .

Table 5.46 contains the result obtained by GA-R3 for Breast Multi Data B. The total number of data points wrongly clustered is 17. The overall accuracy obtained for Breast Multi Data B using GA-R3 was 53.125 % .

Table 5.47 contains the result obtained by GA-R3 for DLBCL A. The total number of data points wrongly clustered is 33. The overall accuracy obtained for DLBCL A using GA-R3 was 76.6 %.

Table 5.48 contains the result obtained by GA-R3 for DLBCL B. The total number of data points wrongly clustered is 38. The overall accuracy obtained for DLBCL B using GA-R3 was 78.89 % .

Table 5.49 contains the result obtained by GA-R3 for DLBCL C. The total number of data points wrongly clustered is 9. The overall accuracy obtained for DLBCL C using GA-R3 was 84.48 % .

Table 5.50 contains the result obtained by GA-R3 for DLBCL D The total number of data points wrongly clustered is 49. The overall accuracy obtained for DLBCL D using GA-R3 was 62.01 % .

Table 5.51 contains the result obtained by GA-R3 for Lung Cancer. The total number of data points wrongly clustered is 41. The overall accuracy obtained for Lung Cancer using GA-R3 was 79.2 %.

Table 5.52 contains the result obtained by GA-R3 for Leukemia Cancer. The total number of data points wrongly clustered is 32. The overall accuracy obtained for Leukemia Cancer using GA-R3 was 55.56%.

Table 5.53 contains the result obtained by GA-R3 for St. Jude Leukemia Cancer. The total number of data points wrongly clustered is 29. Notably cluster 2 and cluster 6 achieves accuracy 100%. The overall accuracy obtained for St. jude Leukemia Cancer using GA-R3 was 88.31 %.

Table 5.54 contains the result obtained by GA-R3 for Cho data. The total number of data points wrongly clustered is 133. The overall accuracy obtained for Cho data using GA-R3 was 65.54 %.

Table 5.55 contains the result obtained by GA-R3 for Iyer data. The total number of data points wrongly clustered is 248. The overall accuracy obtained for Iyer data using GA-R3 was 52.03 %.

Table 5.43: Result of Breast data A (GA-R3)

Breast data A				
	Cluster 1	Cluster 2	Cluster 3	Total
The right number of data point	11	51	36	98
Details of Data points wrongly clustered	5 6 7 8 11	20 31 38 39 46 56	66 80 81	5 6 7 8 11 20 31 38 39 46 56 66 80 81
number of data point wrongly clustered	5	6	3	14
The number of data point correctly clustered	6	45	33	84
Accuracy (%)	54.55	88.24	91.67	85.71

Table 5.44: Result of Breast data B (GA-R3)

Breast data B					
	Cluster 1	Cluster 2	Cluster 3	Cluster 4	Total
The right number of data point	12	11	7	19	49
Details of Data points wrongly clustered	NIL	17	28	31 35 36 41 42 47 48 49	17 28 31 35 36 41 42 47 48 49
number of data point wrongly clustered	0	1	1	8	10
The number of data point correctly clustered	12	10	6	11	39
Accuracy (%)	100	90.91	85.71	57.89	79.59

Table 5.45: Result of Breast Multi data A (GA-R3)

Multi Breast data A					
	Cluster 1	Cluster 2	Cluster 3	Cluster 4	Total
The right number of data point	26	26	28	23	103
Details of Data points wrongly clustered	2 15 19 25 26	38	60 70	NIL	2 15 19 25 26 38 60 70
number of data point wrongly clustered	5	1	2	0	8
The number of data point correctly clustered	21	25	26	23	95
Accuracy (%)	80.76	96.15	92.86	100	92.23

Table 5.46: Result of Breast Multi data B (GA-R3)

Multi Breast data B					
	Cluster 1	Cluster 2	Cluster 3	Cluster 4	Total
The right number of data point	5	9	7	11	32
Details of Data points wrongly clustered	1 4 5	12 13	16 19	22 23 26 28 29 30 31 32	1 4 5 12 13 16 19 22 23 26 28 29 30 31 32
number of data point wrongly clustered	3	2	2	8	15
The number of data point correctly clustered	2	7	5	3	17
Accuracy (%)	40	77.78	71.43	27.27	53.125

Table 5.47: Result of DLBCL A (GA-R3)

DLBCL A				
	Cluster 1	Cluster 2	Cluster 3	Total
The right number of data point	49	50	42	141
Details of Data points wrongly clustered	3 4 9 15 16 22 24 29 43 44 45 46 48	51 62 76 78 93 95 97 98	113 115 118 120 128 130 134 136 137 138 140 141 3 4 9 15 16 22 24 29 43 44 45 46 48 51 62 76 78 9	3 95 97 98 113 115 118 120 128 130 134 136 137 138 140 141
number of data point wrongly clustered	13	8	12	33
The number of data point correctly clustered	36	42	30	108
Accuracy (%)	73.47	84	71.43	76.6

Table 5.48: Result of DLBCL B (GA-R3)

DLBCL B				
	Cluster 1	Cluster 2	Cluster 3	Total
The right number of data point	42	51	87	180
Details of Data points wrongly clustered	2 3 5 14 15 16 32 34 35 36 37 39 40 41	43 46 47 49 51 53 58 60 62 64 65 77 79 92	96 97 103 119 121 122 124 164 167 179	2 3 5 14 15 16 32 34 35 36 37 39 40 41 43 46 47 49 51 53 58 60 62 64 65 77 79 92 96 97 103 119 121 122 124 164 167 179
number of data point wrongly clustered	14	14	10	38
The number of data point correctly clustered	28	37	77	142
Accuracy (%)	66.67	72.55	88.51	78.89

Table 5.49: Result of DLBCL C (GA-R3)

DLBCL C					
	Cluster 1	Cluster 2	Cluster 3	Cluster4	Total
The right number of data point	17	16	13	12	58
Details of Data points wrongly clustered	12	NIL	35 38 40 41 42 43 45	47	12 35 38 40 41 42 43 45 47
number of data point wrongly clustered	1	0	7	1	9
The number of data point correctly clustered	16	16	6	11	49
Accuracy (%)	94.11	100	46.15	91.67	84.48

Table 5.50: Result of DLBCL D (GA-R3)

DLBCL D					
	Cluster 1	Cluster 2	Cluster 3	Cluster4	Total
The right number of data point	19	37	24	49	129
Details of Data points wrongly clustered	1 7 9 13 14 17 19	20 28 30 32 40 41 42 43 45 48 51 56	63 64 65 66 68	81 82 83 84 85 86 87 88 89 90 91 92 93 94 95 96 97 98 100 104 105 108 112 114 117	1 7 9 13 14 17 19 20 28 30 32 40 41 42 43 45 48 51 56 63 64 65 66 68 81 82 83 84 85 86 87 88 89 90 91 92 93 94 95 96 97 98 100 104 105 108 112 114 117
number of data point wrongly clustered	7	12	5	25	49
The number of data point correctly clustered	12	25	19	24	80
Accuracy (%)	63.16	67.57	79.17	48.98	62.01

Table 5.51: Result of Lung Cancer (GA-R3)

	Lung Cancer				
	Cluster 1	Cluster 2	Cluster 3	Cluster4	Total
The right number of data point	139	17	21	20	197
Details of Data points wrongly clustered	15 18 19 20 21 24 26 33 42 50 68 69 71 76 78 79 86 89 90 92 93 97 104 105 109 111 112 114 117 126 135 137 139	144	157 162 167 168 169 174	196	15 18 19 20 21 24 26 33 42 50 68 69 71 76 78 79 86 89 90 92 93 97 104 105 109 111 112 114 117 126 135 137 139 144 157 162 167 168 169 174 196
number of data point wrongly clustered	33	1	6	1	41
The number of data point correctly clustered	106	16	15	19	156
Accuracy (%)	76.26	94.11	71.43	95	79.2

Table 5.52: Result of Leukemia (GA-R3)

	Leukemia		
	Cluster 1	Cluster 2	Total
The right number of data point	47	25	72
Details of Data points wrongly clustered	6 7 8 19 22 23 28 31 32 33 34 35 36 39 40 41 42 45	48 50 51 52 53 54 55 56 57 58 59 61 69 71	6 7 8 19 22 23 28 31 32 33 34 35 36 39 40 41 42 45 48 50 51 52 53 54 55 56 57 58 59 61 69 71
number of data point wrongly clustered	18	14	32
The number of data point correctly clustered	29	11	40
Accuracy (%)	61.70	44	55.56

Table 5.53: Result of St. Jude Leukemia (GA-R3)

	St. Jude Leukemia						
	Cluster 1	Cluster 2	Cluster 3	Cluster4	Cluster5	Cluster6	Total
The right number of data point	15	27	64	20	43	79	248
Details of Data points wrongly clustered	2	NIL	43 48 49 50 58 61 62 69 71 72 74 76 86 91 93 96 97 99 102 103	109 110 111 112	127 131 157 168	NIL	2 43 48 49 50 58 61 62 69 71 72 74 76 86 91 93 96 97 99 102 103 109 110 111 112 127 131 157 168
number of data point wrongly clustered	1	0	20	4	4	0	29
The number of data point correctly clustered	14	27	44	16	39	79	219
Accuracy (%)	93.33	100	68.75	80	90.7	100	88.31

Table 5.54: Result of Cho Data (GA-R3)

Cho Data						
	Cluster 1	Cluster 2	Cluster 3	Cluster4	Cluster5	Total
The right number of data point	67	135	75	54	55	386
Details of Data points wrongly clustered	2 6 25 26 28 29 32 43 45 56 64 66	82 90 96 110 112 125 127 128 129 130 133 134 137 146 173 176 178 180 181 187 188 189 190 191 199	203 205 206 207 210 212 213 214 215 217 218 219 220 221 222 225 226 227 228 229 231 236 237 238 239 241 243 246 247 248 249 250 251 254 255 256 257 258 259 260 261 262 263 268 269 270 272 273 276 277	278 279 281 282 285 286 287 289 290 291 292 293 294 295 296 297 298 299 300 301 302 303 304 305 306 307 308 309 310 311 312 314 315 316 317 318 321 322 324 325 326	332 342 347 354 359 361 366 370	2 6 25 26 28 29 32 43 45 56 64 66 82 90 96 110 112 125 127 128 129 130 133 134 137 146 173 176 178 180 181 187 188 189 190 191 199 203 205 206 207 210 212 213 214 215 217 218 219 220 221 222 225 226 227 228 229 231 236 237 238 239 241 243 246 247 248 249 250 251 254 255 256 257 258 259 260 261 262 263 268 269 270 272 273 276 277 278 279 281 282 285 286 287 289 290 291 292 293 294 295 296 297 298 299 300 301 302 303 304 305 306 307 308 309 310 311 312 314 315 316 317 318 321 322 324 325 326 332 342 347 354 359 361 366 370
number of data point wrongly clustered	9	25	50	41	8	133
The number of data point correctly clustered	58	110	25	13	47	253
Accuracy (%)	86.57	81.481	33.33	31.71	87.04	65.544

Table 5.55: Result of Iyer Data (GA-R3)

Iyer Data					
	The right number of data point	Details of Data points wrongly clustered	Number of data point wrongly clustered	The number of data point correctly clustered	Accuracy (%)
Cluster1	33	1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 21 22 23 28 29 30 31	26	7	78.79
Cluster2	100	NIL	0	100	100
Cluster3	145	143 146 157 161 162 163 164 166 167 168 169 170 171 172 173 174 175 176 177 178 179 180 181 186 187 188 190 191 192 193 194 197 198 199 200 201 202 203 204 206 210 211 213 224 225 226 231 243 244 245 248 249 255 265 267 270 271 273 274 275 278	61	84	57.93
Cluster4	34	280 283 284 285 286 287 294 295 296 297 298 299 300 301 303	15	19	55.88
Cluster5	43	313 314 315 316 317 318 319 320 321 322 324 325 326 327 328 329 330 331 332 333 334 335 342 343 348 349 352 355	28	15	34.89
Cluster6	7	359	1	6	85.71
Cluster7	34	365 366 367 370 373 378 379 381 383 384 387 388 389 390 391 392 393	17	17	50
Cluster8	14	399 401	2	12	85.71
Cluster9	63	411 412 413 414 415 416 417 418 419 420 421 422 423 424 426 427 428 429 430 431 432 433 434 436 437 438 439 440 442 443 444 445 447 448 449 450 451 452 453 454 455 456 457 458 459 460 461 462 463 464 465 466 467 468 469 473	56	7	11.11
Cluster10	19	474 475 476 477 478 479 480 481 482 483 484 485 486 487 488 489 490 492	18	1	5.26
Cluster11	25	493 494 495 496 497 498 499 500 502 503 504 505 506 507 508 509 510 511 512 513 514 515 516 517	24	1	4
Total	517	1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 21 22 23 28 29 30 31 143 146 157 161 162 163 164 166 167 168 169 170 171 172 173 174 175 176 177 178 179 180 181 186 187 188 190 191 192 193 194 197 198 199 200 201 202 203 204 206 210 211 213 224 225 226 231 243 244 245 248 249 255 265 267 270 271 273 274 275 278 280 283 284 285 286 287 294 295 296 297 298 299 300 301 303 313 314 315 316 317 318 319 320 321 322 324 325 326 327 328 329 330 331 332 333 334 335 342 343 348 349 352 355 359 365 366 367 370 373 378 379 381 383 384 387 388 389 390 391 392 393 399 401 411 412 413 414 415 416 417 418 419 420 421 422 423 424 426 427 428 429 430 431 432 433 434 436 437 438 439 440 442 443 444 445 447 448 449 450 451 452 453 454 455 456 457 458 459 460 461 462 463 464 465 466 467 468 469 473 474 475 476 477 478 479 480 481 482 483 484 485 486 487 488 489 490 492 493 494 495 496 497 498 499 500 502 503 504 505 506 507 508 509 510 511 512 513 514 515 516 517	248	269	52.03

Final fitness value after convergence of GA-R1, GA-R2 and GA-R3 based clustering algorithms has been tabulated in Table 5.56. GA-R1 attains minimum fitness value in case of Iyer, Breast data B and Breast Multi data A. GA-R2 attains minimum fitness value in case of Leukemia, Breast Multi Data B, DLBCL C, DLBCL D and Lung Cancer. GA-R3 attains minimum fitness value in case of Cho Data, Breast Data A, DLBCL A, DLBCL B and St. jude Leukemia data. It may be noted that GA-R2 and GA-R3 attains same fitness value for Iyer data (i.e., 48.3397) but minimum fitness value was attained by GA-R1 (i.e., 47.6926). GA-R1 and GA-R2 attains minimum fitness value for Breast Data B and it is optimal compared to GA-R3. Also, GA-R1 and GA-R2 attains same minimum fitness value for Breast Multi Data A and it is optimal compared to GA-R3.

Table 5.56: Final Fitness Function value for Bioinformatics Data

Dataset Sl. No.	**Datasets**	GA-R1	GA-R2	GA-R3
3	**Iyer data/Serum data**	0.02096	0.02068	0.02068
4	**Cho data (yeast data)**	0.02146	0.02157	0.02397
5	**Leukemia (Golub Experiment)**	0.10374	0.12475	0.10965
6	**Breast data A**	0.11518	0.10594	0.11548
7	**Breast data B**	0.33563	0.33563	0.33242
8	**Breast Multi data A**	0.09014	0.09014	0.0895
9	**Breast Multi data B**	0.18350	0.23075	0.2247
10	**DLBCL A**	0.06406	0.06410	0.06841
11	**DLBCL B**	0.06150	0.06207	0.06311
12	**DLBCL C**	0.18437	0.19119	0.18194
13	**DLBCL D**	0.14457	0.15479	0.1426
14	**Lung Cancer**	0.03538	0.03675	0.03538
15	**St. Jude Leukemia data**	0.04475	0.04454	0.04512

Table 5.57 summarizes the accuracy of GA based clustering algorithm for bioinformatics data. Average, best and worst case analysis has been carried out on bioinformatics data for GA-R1, GA-R2 and GA-R3. As far as best case analysis is concerned, GA-R1 performs better in case of Iyer data, Breast multi data A, DLBCL B data ; GA-R3 performs better in case of Iris, Breast data B, DLBCL A, DLBCL C and in rest of cases GA-R2 performs better compared to GA-R1 and GA-R3 (Table 5.57).

Table 5.57: Comparison of GA based clustering algorithm for Bioinformatics data using Accuracy

Dataset Sl. No.	**Datasets**	**# Samples/genes**	**GA-R1**		**GA-R2**		**GA-R3**	
			# correct	Accuracy(%)	# correct	Accuracy(%)	# correct	Accuracy(%)
3	Iyer data/Serum data	517	269	**52.0309**	266	51.4507	266	51.4507
4	Cho data (yeast data)	386	259	67.0984	287	**74.3523**	250	64.7668
5	Leukemia (Golub Experiment)	72	40	55.566	50	**69.4444**	40	55.566
6	Breast data A	98	88	89.7959	91	**92.8571**	84	85.7143
7	Breast data B	49	38	77.5510	38	77.5510	39	**79.5918**
8	Breast Multi data A	103	100	**97.0874**	100	97.0874	95	92.2330
9	Breast Multi data B	32	20	62.5000	23	**71.8750**	17	53.1250
10	DLBCL A	141	98	69.5035	92	65.2482	108	**76.5957**
11	DLBCL B	180	152	**84.4444**	147	81.6667	142	78.8889
12	DLBCL C	58	46	79.3103	40	68.9655	50	**86.2069**
13	DLBCL D	129	85	65.8915	93	**72.0930**	80	62.0155
14	Lung Cancer	197	156	79.1878	165	**83.7563**	156	79.1878
15	St. Jude Leukemia data	248	233	93.9516	235	**94.7581**	219	88.3065

5.4 Comparative Studies on HCM, SCM and GA based Clustering Algorithm

To evaluate performance of HCM, SCM and GA based clustering algorithm; Clustering Accuracy was used as cluster validation metric. Extensive computer simulation (Table 5.57) shows that GA based clustering algorithm was able to provide the highest accuracy and generalization results compared to Non-GA based clustering Algorithm in all cases. Average, best and worst case analysis have been also carried out on machine learning data as well as bioinformatics data. Soft C-means shows superior performance in 11 cases (Iris, WBCD, Cho/yeast data, Breast data A, Breast data B, Breast Multi data A, DLBCL A, , DLBCL C, DLBCL D, Lung Cancer, St. Jude Leukemia data) over Hard C-means algorithm; while Hard C-mean shows superior performance in 4 cases (Iyer/serum, Leukemia, Breast Multi data B, DLBCL B) over Soft C-means (Table 5.58).

GA based clustering algorithm always shows superior performance compared to Non-GA based clustering algorithm. As far as best case analysis is concerned, GA-R1 performs better in case of Iyer data, Breast multi data A, DLBCL B data ; GA-R3 performs better in case of Iris, Breast data B, DLBCL A, DLBCL C and in rest of cases GA-R2 performs better compared to GA-R1 and GA-R3 (Table 5.58).

Table 5.58: Comparison of HCM, SCM and GA based clustering algorithm for all fifteen data using Accuracy

Sl. No.	**Datasets**	**# Samples**	**Hard C-means**		**Soft C-means**		**GA-R1**		**GA-R2**		**GA-R3**	
			# correct	Accuracy(%)	# correct	Accuracy(%)	# correct	Accuracy(%)	# correct	Accuracy(%)	# correct	Accuracy(%)
1	Iris	150	133	88.67	136	90.67	140	93.33	144	96	150	**100**
2	WBCD	683	654	95.75	656	96.05	657	96.1933	661	96.7789	665	97.3646
3	Iyer data/Serum data	517	268	51.84	252	48.74	269	**52.0309**	266	51.4507	266	51.4507
4	Cho data (yeast data)	386	235	60.88	246	63.73	259	67.0984	287	**74.3523**	250	64.7668
5	Leukemia (Golub Experiment)	72	43	59.72	40	55.56	40	55.566	50	**69.4444**	40	55.566
6	Breast data A	98	71	72.44	86	87.75	88	89.7959	91	**92.8571**	84	85.7143
7	Breast data B	49	26	53.06	32	65.30	38	77.5510	38	77.5510	39	**79.5918**
8	Breast Multi data A	103	82	79.61	93	90.29	100	**97.0874**	100	97.0874	95	92.2330
9	Breast Multi data B	32	17	53.125	16	50	20	62.5000	23	**71.8750**	17	53.1250
10	DLBCL A	141	75	53.191	83	58.86	98	69.5035	92	65.2482	108	**76.5957**
11	DLBCL B	180	140	77.78	136	75.56	152	**84.4444**	147	81.6667	142	78.8889
12	DLBCL C	58	30	51.7241	44	75.86	46	79.3103	40	68.9655	50	**86.2069**
13	DLBCL D	129	55	42.64	65	50.38	85	65.8915	93	**72.0930**	80	62.0155
14	Lung Cancer	197	142	72.0812	150	76.14	156	79.1878	165	**83.7563**	156	79.1878
15	St. Jude Leukemia data	248	211	85.08	219	88.31	233	93.9516	235	**94.7581**	219	88.3065

5.5 Conclusion

In this chapter, four different types of encoding schemes for chromosome have been studied for clustering. GA based clustering algorithm overcomes the limitation of HCM and SCM clustering algorithm (i.e., to get trapped in local optimum solution). Extensive computer simulation shows that GA based clustering algorithm was able to provide the highest accuracy and generalization results compared to Non-GA based clustering algorithm (HCM and SCM) in all fifteen cases.

As far as best case analysis is concerned, GA-R1 performs better in case of Iyer data, Breast multi data A, DLBCL B data; GA-R3 performs better in case of Iris, Breast data B, DLBCL A, DLBCL C and in rest of cases GA-R2 performs better compared to GA-R1 and GA-R3.

As far as memory utilization is concerned, it is advisable to go for GA-R2 clustering algorithm when number of features are less in number in a dataset otherwise to go for GA-R1 clustering algorithm.

Chapter 6

Brute Force based Clustering And Simulated Annealing based Preprocessing of Data

This chapter is broadly divided into two section:

- An incremental Brute-Force approach for Clustering and
- Preprocessing (diversification) of data using Simulated Annealing (SA).

6.1 An Incremental Brute-Force Approach for Clustering

The Brute-Force approach for clustering was intended for three specific purposes. These are as follows:

- It should not require information like no. of clusters from user i.e it should help in automatic evolution of clusters.
- It should be computationally faster so that it may be useful for high dimensional data.
- It should be efficient in nature in terms of cluster formation.

The main steps involved in the proposed approach are shown in fig. 6.1.

Algorithmic Steps of An incremental Brute-Force Approach for Clustering:

Given a piece of gene expression data: **the first step** is Data preprocessing. In general, it can be done by simple transformation or normalization performed on single variables, filters and calculation of new variables from existing ones. In proposed work, only the

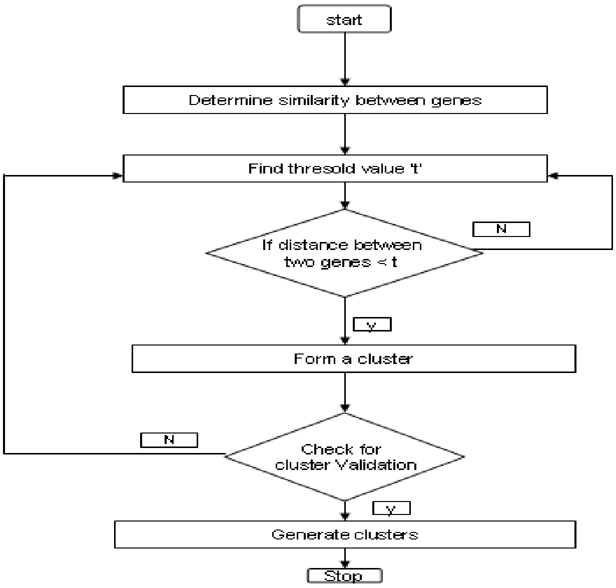

start
Determine similarity between genes
Find thresold value 't'
If distance between two genes < t
N
y
Form a cluster
Check for cluster Validation
N
y
Generate clusters
Stop

Figure 6.1: Flow-Chart of Brute-Force Approach based Clustering Algorithm

first of these is implemented. Scaling of variables is of special importance, say for example, Euclidean metric has been used to measure distances between vectors. If one variable has values in the range of 0,...,1000 and another in the range of 0,...,1 the former will almost completely dominate the cluster formation because of its greater impact on the distances measured. Typically, one would want the variables to be equally important. The standard way to achieve this is to linearly scale all variables so that their variances are equal to one [93].

Second step, is to compute Distance matrix ‘D’ from processed data obtained in step first. ‘D_{ij}’ represents the distance between the expression patterns for genes ‘i’ and ‘j’. Although a number of alternative measures could be used to calculate the similarity between gene expressions, Euclidean distance metric [7], [8], [9], [10] has been used due to its wide application range.

In the Third step, a threshold value, called ‘θ’, is computed as follows:

‘$\theta = z \times$ Average distance between genes’, where ’z’ is a positive constant. The value of ‘z’ is chosen in such a way that number of clusters lies between $2\ to\ \sqrt{n}$. Lesser the value of ‘z’, more the number of clusters. ‘θ’ is calculated based on distance matrix, that generates no. of cluster automatically. This threshold value is computed dynamically and changes after each cluster formation. This depends on two factor, first, the average similarity of whole gene and secondly, how many genes are left for next cluster formation.

Fourth step is an iterative step. If distance between two genes are less than threshold value 'θ', it forms a first cluster otherwise it falls under second cluster . This step is repeated iteratively unless all the genes fall under some particular clusters.

In the final step, a validation test is performed to evaluate the quality of the clustering result produced in step fourth.

6.1.1 Experimental Evaluation

This section describes about the experimental setup and datasets used for carrying the simulation performance of an incremental Brute-Force approach for clustering.

1. **Experimental Setup**

   To validate the feasibility and performance of the proposed approach, implementation has been done in MATLAB 7.0 (C2D, 2.0 GHz, 2 GB RAM) and applied it to both of real gene expression data and synthetic data.

2. **Datasets**

   To evaluate the performance of proposed approach, two real and one synthetic gene expression data has been considered for study. These datasets do not possess referenced (class-labeled) information available to the data.

   - **Datasets I** is a synthetic data of [10x3] matrix.
   - **Datasets II** represents Wisconsin breast cancer dataset and is obtained from the University Medical Centre, Institute of Oncology, Ljubljana, Yugoslavia (*http://mlearn.ics.uci.edu or ftp://ftp.ics.uci.edu/pub/machine-learning-databases/breast- cancer-wisconsin*). The dataset contains 699 instances and each instances are having 9 features. There are 16 datapoints with missing values. Missing values have been replaced by mean of the feature of column in which missing value was found.

- **Datasets III** is a real biological microarray data of [118x60] matrix that represents growth inhibition factors when 118 drugs with putatively understood methods of action were applied to the NCI60 cell lines. The original data can be downloaded from *http://discover.nci.nih.gov/nature2000/data/selected_data/a_matrix118.txt.*

6.1.2 Cluster Validation Metrics

Since all the datasets (Datasets I, II and III) considered in this chapter for simulation study do not possess class-labeled information, clustering accuracy can not be used as a cluster validation metric. In this chapter of the thesis, HS_Ratio [45], [20], [13] is used as cluster validation metric to validate the quality of clusters. Details of the HS_Ratio has been already discussed in section 5.2.3. It may be noted that "*the quality of cluster V increases with higher homogeneity values within C and lower separation values between V and other clusters*".

6.1.3 Results and Discussion

Brute-Force based clustering approach has been simulated for different value of 'z' and result obtained were tabulated in Table 6.1. The value of parameter 'z' has been taken in range $\{0.3, 1.8\}$ for simulation studies. The algorithm generates number of cluster automatically. The quality of the clusters formed were assessed using HS_Ratio.
The simulation results shown in Table 6.2 show that the proposed Brute-Force based clustering approach may perform better compared to HCM clustering algorithm when the no. of cluster is high.
Table 6.3 shows the proposed Brute Force based Clustering approach is computationally quite faster than conventional HCM clustering algorithm(fig. 6.2) and thus it may be very useful while dealing with high dimensional microarray data.

Another important feature of the proposed Brute-Force based clustering approach in opposite to HCM clustering algorithm is that, unlike HCM Clustering algorithm it does not require the value of number of cluster i.e., 'C' from user.

Table 6.1: HS _Ratio value for Brute-Force approach based clustering

Brute-Force Approach based Clustering Algorithm							
-	Trial No	z	θ	No of cluster	$H_{average}$	$S_{average}$	HS _Ratio
Sample data [10 X 3]	1	0.3000	2.383434e+000	5	0.1425	0.3047	0.4676
	2	.7	7.944781e+000	3	0.2877	0.1119	2.5706
	3	0.7000	5.561347e+000	4	0.2189	0.3073	0.7122
	4	1.2000	9.533738e+000	2	0.5233	0.1569	3.3343
	5	1.3	1.032822e+001	2	0.4649	0.8592	0.5411
	6	1.4000	1.112269e+001	2	0.4649	0.8592	0.5411
Breast Cancer [699 X 9]	1	.9500	9.551604e+000	24	0.4889	0.5077	0.9630
	2	1	1.005432e+001	20	0.5946	0.5644	1.0535
	3	1.05	1.055704e+001	15	0.8097	0.5338	1.5168
	4	1.1000	1.105975e+001	12	1.0299	0.6057	1.7003
	5	1.2000	1.206518e+001	8	1.5935	0.6174	2.5808
	6	1.4	1.407605e+001	4	3.2558	0.5732	5.6799
	7	1.6000	1.608691e+001	3	4.5015	0.5290	7.9747
	8	1.8000	1.809778e+001	2	6.8196	0.2794	24.4060
Cancer Data [118 X 60]	1	0.7000	1.146838e+001	9	0.5360	0.8097	0.6620
	2	0.7300	1.195988e+001	8	0.6351	0.7892	0.8047
	3	1	1.638340e+001	5	1.1719	0.8240	1.4221
	4	1.1000	1.802174e+001	4	1.5445	0.5712	1.5592
	5	1.6000	2.621344e+001	3	2.3853	0.4399	2.1310

Table 6.2: Comparative study on HCM and Brute Force approach based clustering

	No. Of Cluster	HCM clustering algorithm	Brute Force Approach
Sample data [10 X 3]	3	2.7195	2.5706
	2	3.3343	0.5411
Breast Cancer [699 X 9]	20	0.4899	**1.0535**
	15	0.5881	**1.5168**
	12	1.0293	**1.7003**
	8	1.9899	**2.5808**
	4	6.3689	5.6799
	3	8.5102	7.9747
	2	38.1630	24.4060
Cancer Data [118 X 60]	9	0.5595	**0.6620**
	8	0.5522	**0.8047**
	5	1.0069	**1.1043**
	4	2.7040	1.5592
	3	5.4224	2.1310

Table 6.3: Computational time for HCM and Brute-Force based clustering Algorithm

Datasets	Data Size	HCM clustering Algorithm	Brute-Force based clustering
Sample data	[10x3] Matrix	0.0203 Second	**0.0008** Second
Breast Cancer	[699x9] Matrix	0.5 Second	**0.344** Second
Cancer Data	[118x60] Matrix	0.047 Second	**0.0310** Second

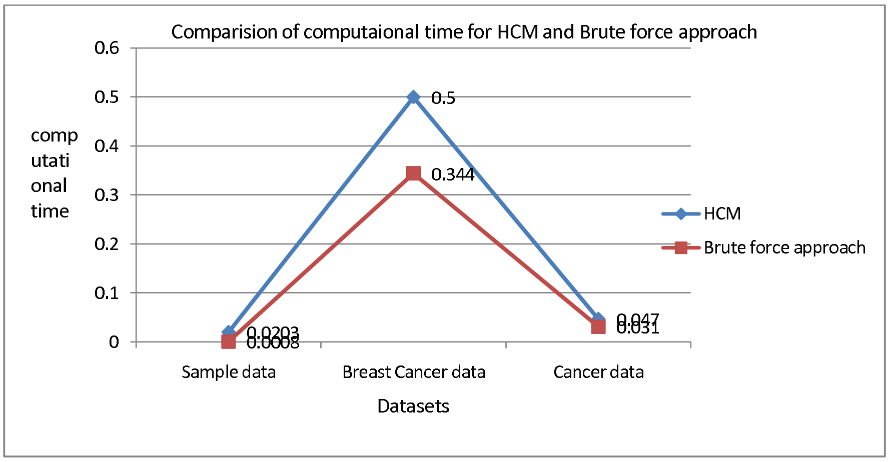


Figure 6.2: Comparison of Computational time for HCM and Brute-Force apraoach based clustering

6.1.4 Conclusion

In this section of the thesis, a Brute-Force approach based clustering has been proposed. Performance evaluation of proposed approach has been compared with conventional HCM clustering Algorithm using artificial/synthetic and real datasets (machine learning as well as bioinformatics data). Simulation results obtained shows that the proposed approach can achieve a high degree of automation and efficiency. The proposed approach does not require the value of number of cluster '*C*' from user. The proposed approach is also quite faster than HCM clustering algorithm and thus it could be useful for high dimensional microarray data. As far as efficiency is concerned, proposed Brute-Force based clustering approach may perform better compared to HCM clustering algorithm when the no. of clusters are higher in value.

6.2 Preprocessing of Data using Simulated Annealing

Simulated Annealing (SA) exploits an analogy between the way in which a metal cools and freezes into a minimum energy crystalline structure (the annealing process) and the search for a minimum in a more general system. Kirkpatrick et. al. [12] was first, who proposed that SA form the basis of an optimization technique for combinatorial and optimization problems. It has been proved that by carefully controlling the rate of cooling of the temperature, SA [12] can find the global optimum. SA's major advantage over other methods is its ability to avoid becoming trapped in local minima. The algorithm employs a random search which not only accepts changes that decreases the objective function 'f' (assuming a minimization problem), but also some changes that increase it. The latter are accepted with a probability $p = exp(-df/T)$, where 'df' is the increase in 'f' and 'T' is a control parameter, which by analogy with the original application is known as the system '$Temperature$' irrespective of the objective function involved.

6.2.1 Purpose of the Proposed algorithm

The proposed method was meant for the specific purpose, to show how diversification (preprocessing) of the data may improve efficiency of the clustering algorithm. The method gives emphasis on clustering efficiency. Since SA (a meatheuristic) has been used in proposed approach, clustering efficiency has been achieved at the cost of computational time.

6.2.2 Basic steps involved in SA based clustering

The main steps of the proposed approach are as follows: Given a piece of gene expression data, **the first step** is Data preprocessing.

Second step is to diversify the data using Simulated Annealing method. The implementation of the basic SA algorithm is shown in fig. 6.3.

In **third step**, any clustering technique e.g., HCM clustering algorithm) may be used for cluster formation.

In the final step, a validation test is performed to evaluate the quality of the clustering result produced in third step.

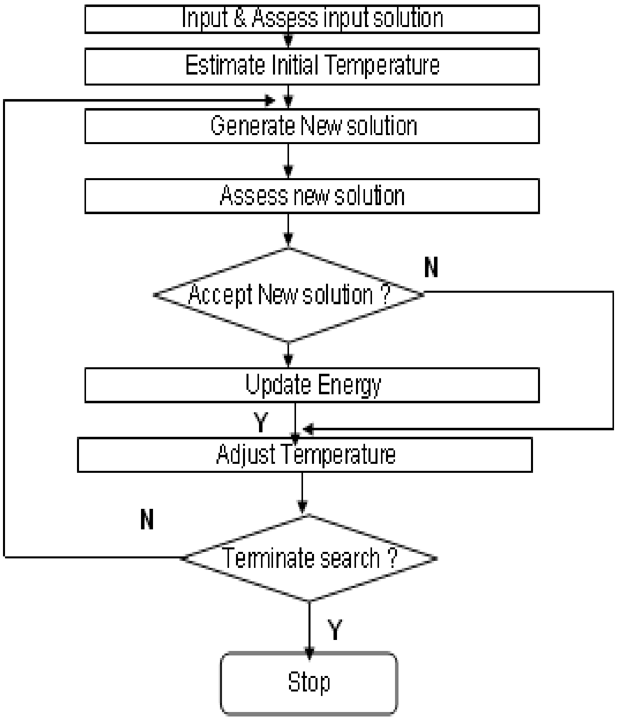


Figure 6.3: Flow-Chart for diversification of Dataset using SA

6.2.3 Experimental Evaluation

To evaluate the performance of proposed approach, the same experimental condition and same datasets which are used for Brute-Force approach based clustering (**section 6.1.1**), two real and one synthetic gene expression data has been used for study.

Parameters used for SA are shown in Table 6.4.

Table 6.4: Parameters used in Simulated Annealing

Parameter	Value
No. of iteration	1000 × No. Of Genes/samples
Stopping criterion	99.9
Geometrical cooling (α)	.9
Learning rate (l)	1

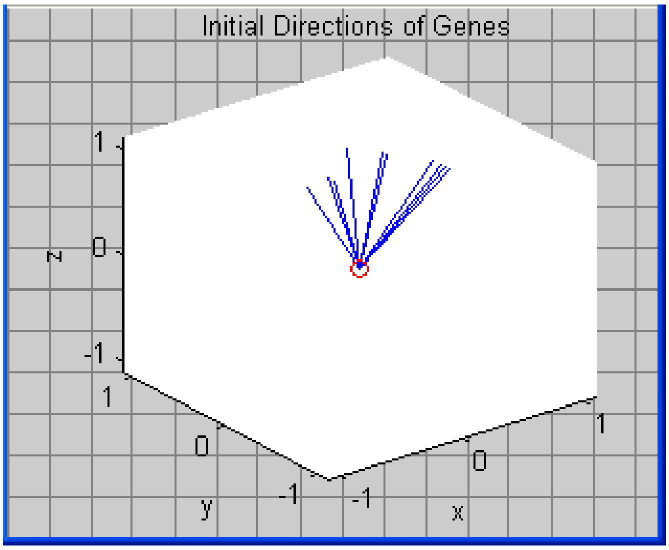


Figure 6.4: Initial Unit Directions for Datasets I

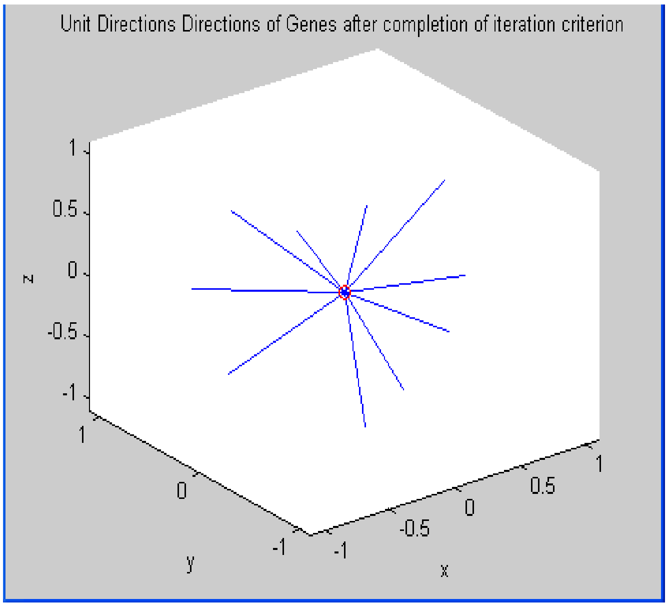


Figure 6.5: Final Unit Directions for Datasets I

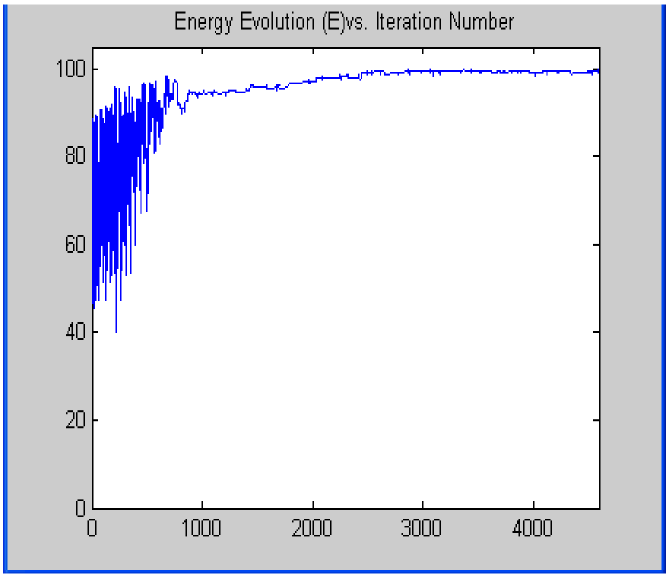


Figure 6.6: Energy evolution for Datasets I

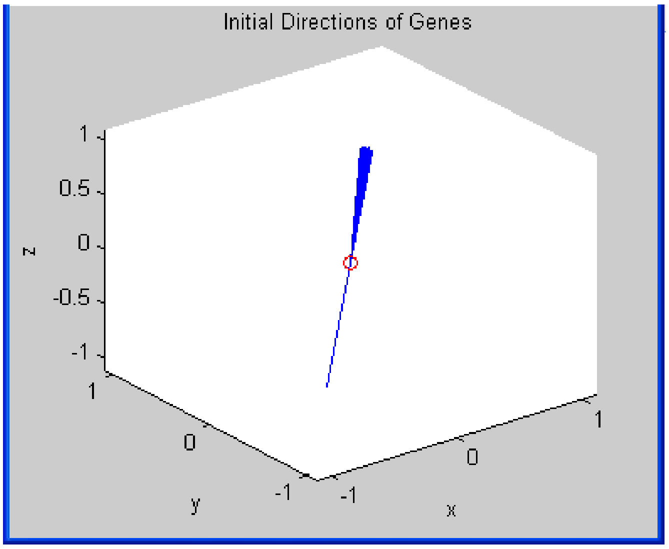


Figure 6.7: Initial Unit Directions for Datasets II

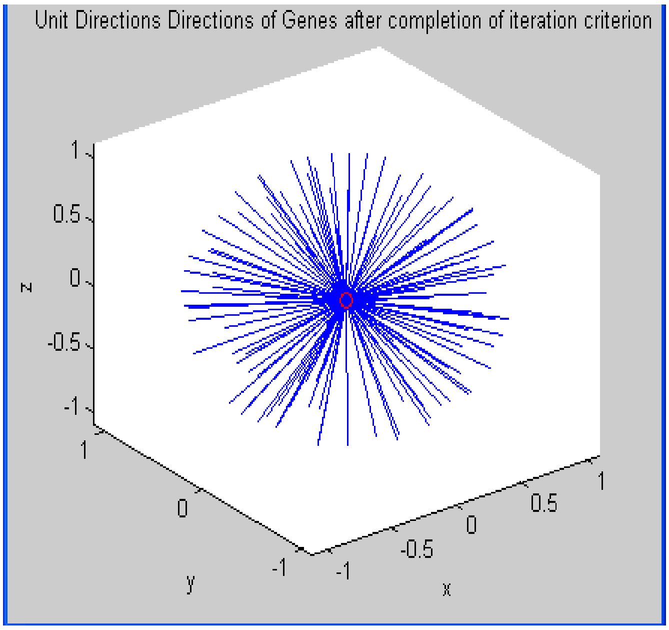


Figure 6.8: Final Unit Directions for Datasets II

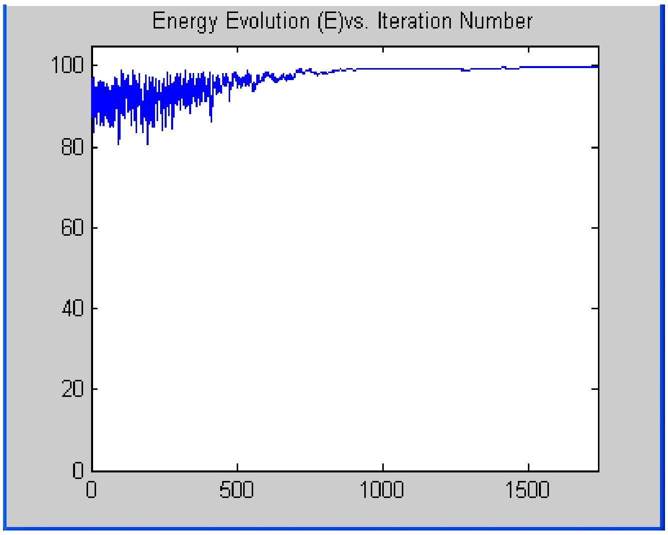


Figure 6.9: Energy evolution for Datasets II

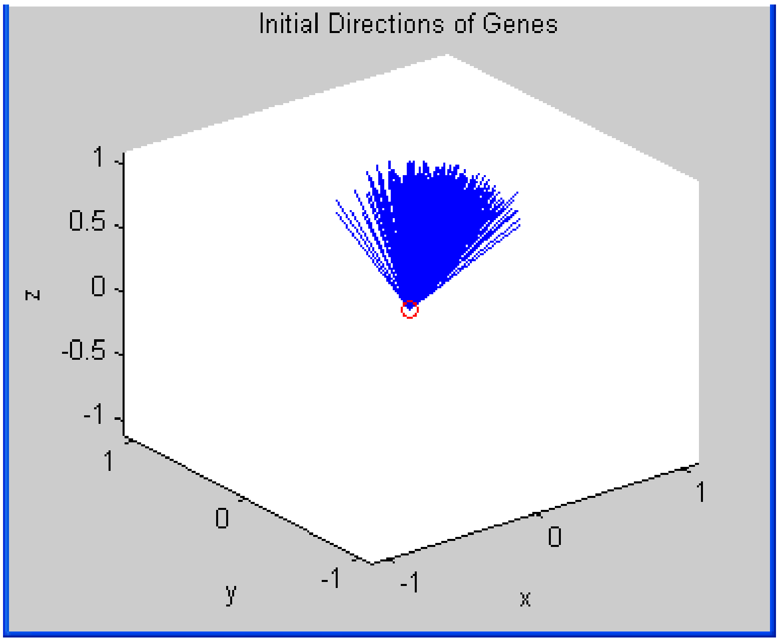


Figure 6.10: Initial Unit Directions for Datasets III

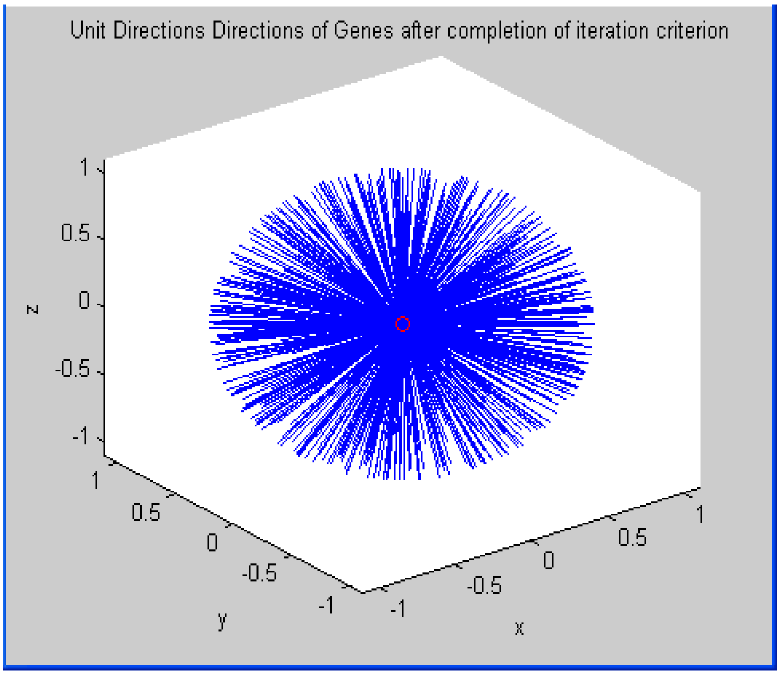


Figure 6.11: Final Unit Directions for Datasets III

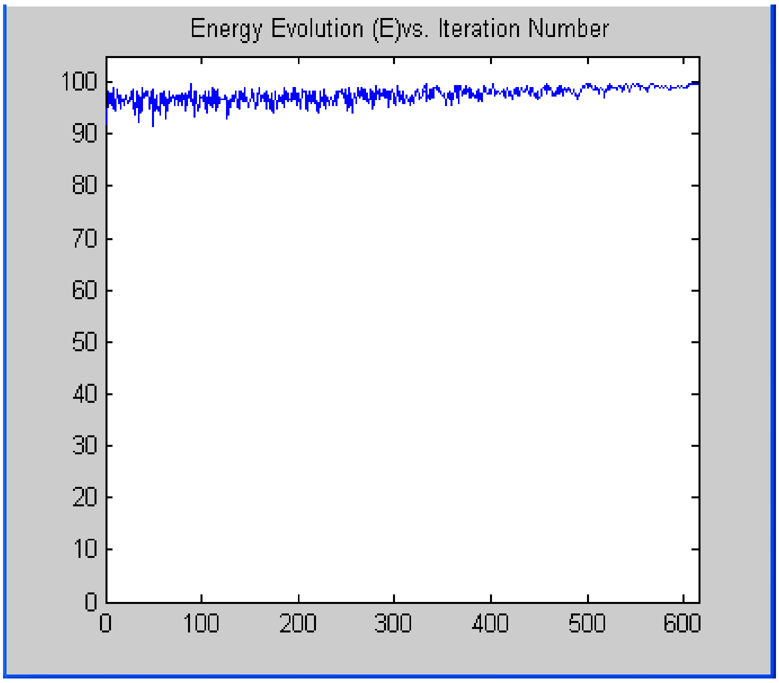


Figure 6.12: Energy evolution for Datasets III

6.2.4 Results and Discussion

Simulation of SA processed based HCM clustering algorithm and HCM clustering algorithm was carried out and result obtained were compared. The quality of the clusters formed were assessed using HS_Ratio.

Fig. 6.4, 6.5, 6.6 shows result of SA on Datasets I.

Fig. 6.7, 6.8, 6.9 shows result of SA on Datasets II.

Fig. 6.10, 6.11, 6.12 shows result of SA on Datasets III.

Fig. 6.4, 6.7, 6.10 represents the unit direction of genes before implementing SA on Datasets I, Datasets II and Datasets III.

Fig. 6.5, 6.8, 6.11 represents the unit direction of genes after implementing SA on Datasets I, Datasets II and Datasets III. These diagrams show that gene were diversified and henceforth results in good cluster formation.

Fig. 6.6, 6.9, 6.12 represents the Energy Evolution of genes Datasets I, Datasets II and Datasets III. These figures show that after 1,000 iteration change in Energy almost becomes constant and this depicts that gene were completely diversified.

The experimental results for Datasets I, II and III have been shown in Table 6.5.

It is evident from Table 6.5 that SA processed based HCM clustering algorithm perform better than HCM clustering.

Table 6.5: Comparative studies on HCM and and SA based HCM Clustering Algorithm

Datasets	**# cluster**	**SA-HCM**			**HCM Algorithm**		
		H	S	HS_Ratio	H	S	HS_Ratio
Sample data	3	.2374	.0711	**3.33**	.319	.1173	2.72
Breast Cancer data	15	.3020	.3518	**.8584**	.4659	.5478	.8504
	20	.2033	.3131	**.6493**	.2908	.6272	.4636
	30	.1156	.316	**.3658**	.1526	.5524	.2762
	40	.0765	.3403	**.225**	.0931	.5901	.1578
cancer data	8	.2696	.2768	**.97**	.463	.894	.52
	10	.2043	.3771	**.5505**	.3582	.8749	.4094
	15	.1185	.3086	**.3839**	.2034	.7829	.2598
	20	.0766	.2930	**.2614**	.1372	.6326	.21688

6.2.5 Conclusion

In this section of the thesis, Simulated Annealing based method for diversification of the data has been proposed. Performance evaluation of *SA based Hard C-means* and conventional Hard C-means clustering algorithm has been compared using artificial / synthetic and real datasets (machine learning as well as bioinformatics data). Results obtained show that the *SA based Hard C-means* can achieve a high degree of accuracy compared to Hard C-means clustering algorithm.

Chapter 7

Performance Evaluation of Clustering Algorithm using Cluster Validation Metrics

In the previous chapters, extensive studies have been done on several clustering algorithms which partition the dataset based on different clustering criteria. For gene expression data, clustering results in groups of co-expressed genes. However, different clustering algorithms, using different parameters, generally result in different sets of clusters. Therefore, it is important to compare various clustering results and select the one that best fits the '*true*' data distribution. Cluster validation is the process of assessing the quality and reliability of the cluster sets derived from various clustering processes. In this chapter, first, summary of several cluster validation metrics available in literature has been presented and next, comprehensive studies have been performed on three cluster validation metrics namely, HS_Ratio, Figure of Merit (FOM) and clustering Accuracy.

7.1 Summary of Cluster Validation Metrics

Table 7.1 summarizes the several cluster validation metrics for clustering algorithm available in literature.

Generally, cluster validity has **three** aspects. **First**, the quality of clusters can be measured in terms of homogeneity and separation on the basis of the definition of a cluster: *"objects within one cluster are similar to each other, while objects in different clusters are dissimilar with each other"*. For this, HS_Ratio has been used as cluster validation metric. The **second** aspect relies on a given '*ground truth*' of the clusters. The

Table 7.1: Cluster Validation

Sl. no.	Validity Index	Source
1	**Homogeneity and separation**	[13], [45], [20]
2	Rand Index	[13], [45], [141], [142] , [143], [144]
3	Jaccard coefficient	[13], [45], [141], [142], [145]
4	Minkowski measure	[13], [45], [141], [142]
5	Adjusted rand index	[144]
6	Wighted rand index	[146]
7	C index	[147]
8	Goodman-Kruskal index	[148]
9	Isolation index	[149]
10	Davies-Bouldin Index	[150], [151]
11	Dunn Index	[150], [83]
12	Generalized Dunn Index	[150], [152]
13	Calinski Harabasz(CH) Index	[150], [153]
14	I index	[150], [154]
15	XB index	[150]
16	Biological Homogeneity Index	[155]
17	Biological stability index	[155]
18	p-Value	[13], [45]
19	Prediction strength	[41]
20	**Figure Of merit**	[13], [45], [156]
21	Silhouette width	[157]
22	Redundant Separation Scores(RSS)	[157]
23	Weighted average discrepant pairs (WADP)	[157]
24	PS	[158], [159]
25	**Cluster Accuracy**	[160]

‘$ground\ truth$’ or ‘$class-labeled\ information$’ could come from domain knowledge, such as known function families of genes, or from other sources such as the clinical diagnosis of normal or cancerous tissues. Cluster validation is based on the agreement between clustering results and the “$ground\ truth$. For this, Cluster Accuracy was used as cluster validation metric. The **third** aspect of cluster validity focuses on the reliability of the clusters, or the likelihood that the cluster structure is not formed by chance. For this, Figure of Merit (FOM) was used as cluster validation metric. In the next subsection, discussion has been made on three aspects of cluster validation metrics in details.

7.1.1 Homogeneity and Separation

This measure is based on the principle *"objects within one cluster are assumed to be similar to each other, while objects in different clusters are dissimilar"*. This cluster validation metric HS_Ratio is already discussed in details in section 5.2.3 ([20], [45]).

7.1.2 Figure of Merit

Yeung et. al. [45], [156] proposed an approach to cluster validation of gene clusters. Intuitively, if a cluster of genes has possible biological significance, then the expression levels of the genes within that cluster should also be similar to each other in '*test*' samples that were not used to form the cluster. Yeung et. al. [45], [156] proposed a specific *figure of Merit (FOM)*, to estimate the predictive power of a clustering algorithm. Suppose $\{V_1, V_2, \ldots, V_C\}$ are the resulting clusters based on samples $\{1, \ldots, (e-1), (e+1), \ldots, n\}$ and sample 'e' is left out to test the prediction strength. Let $R(g,e)$ be the expression level of gene 'g' under sample 'e' in the raw data matrix. Let $\mu_{V_i}(e)$ be the average expression level in sample 'e' of the genes in cluster V_i. The figure of merit with respect to 'e' and the number of cluster 'C' is defined as

$$FOM(e,\ C) = \sqrt{\tfrac{1}{n} \times \textstyle\sum_{i=1}^{C} \sum_{x \in V_i} \left(R(x,e) - \mu V_i(e)\ \right)^2}$$

Each of the n samples can be left out in turn, and the *aggregate figure of merit* is defined as $FOM(C) = \sum_{e=1}^{n} FOM(e,\ C)$. The FOM measures the mean deviation of the expression levels of genes in e relative to their corresponding to cluster means. Thus, "*a small value of FOM indicates a strong prediction strength, and therefore a high level reliability of the resulting clusters*".

7.1.3 Clustering Accuracy

A simple approximation of accuracy for un-supervised learning that employs external class information was described by Topchy et al. (2003). By finding the optimal correspondence between a dataset's annotated class labels and the clusters in a given partition, a performance measure may be derived that reflects the proportion of instances that were correctly assigned. "*A high value for this measure generally indicates a high level of agreement between a clustering and the annotated natural classes*". It may be noted that this measure is only applicable when the number of clusters 'C' is the same as the number of natural classes. Clustering Accuracy is defined as:

$$ClusteringAccuracy = (\frac{Number\ of\ Correct\ Count}{Total\ number\ of\ instances\ genes/samples}) * 100$$

.

7.2 Dataset used For Simulation studies

In this chapter of the thesis, fifteen datasets has been taken for simulation studies. Details about these datasets has been already discussed in section 4.1.1.

7.3 Performance Evaluation Of Clustering Algorithm using Cluster Validation Metrics

In this section, performance evaluation of Hard C-means, Soft C-means and family of GA based clustering algorithm has been studied using three standard cluster validation metrics. These cluster validation metrics are: HS_Ratio, Figure of Merit (FOM) and Clustering accuracy. Table 7.2 contains the result obtained by HS_Ratio for all fifteen datasets.

Table 7.2: Comparison of HCM, SCM and GA based clustering algorithm using *HS_Ratio*

Sl. No.	**Datasets**	**Original**	**HCM**	**SCM**	GA-R1	GA-R2	GA-R3
1	**IRIS**	96.8226	104.4341	102.3522	100.8436	**91.1395**	96.8226
2	**WBCD**	613.2184	629.6011	632.8762	582.6400	**577.7448**	585.7532
3	**Iyer data/Serum data**	46.5158	55.9262	**44.6866**	47.6926	*48.3397*	*48.3397*
4	**Cho data (yeast data)**	40.2317	52.8210	47.9512	46.5921	46.3559	**41.7082**
5	**Leukemia (Golub Experiment)**	8.2935	9.6394	9.1198	9.6394	**8.0156**	9.1198
6	**Breast data A**	10.5446	9.8435	8.7272	8.6815	9.4387	**8.6591**
7	**Breast data B**	3.0897	3.6018	3.2802	**2.9794**	**2.9794**	3.0082
8	**Breast Multi data A**	10.8731	11.7411	*11.1699*	**11.0932**	**11.0932**	*11.1699*
9	**Breast Multi data B**	3.2005	5.5203	5.3186	5.4495	**4.3336**	4.4502
10	**DLBCL A**	13.6649	**13.0831**	16.3963	15.6081	15.6001	14.6159
11	**DLBCL B**	15.3407	16.7588	16.0616	16.2582	16.1106	**15.8453**
12	**DLBCL C**	4.9864	5.9293	5.5618	5.4237	**5.2302**	5.4963
13	**DLBCL D**	6.6913	8.1304	7.9158	6.9168	**6.4602**	7.0126
14	**Lung Cancer**	25.9172	31.3441	29.9749	*28.2616*	**27.2038**	*28.2616*
15	**St. Jude Leukemia data**	22.1020	**19.0021**	22.0266	22.3435	22.4469	22.1592

Table 7.2 contains the result obtained by cluster validation metric based on HS_Ratio. HCM attains minimum value of *HS_Ratio* in case of DLBCL A and St. Jude leukemia data. SCM attains minimum value of *HS_Ratio* in case of Iyer data. GA-R1 attains

minimum value of *HS_Ratio* in case of Breast data B and Breast multi data A. GA-R2 attains minimum value of *HS_Ratio* in case of Iris, WBCD, leukemia, Breast data B, Breast multi data A, Breast multi data B, DLBCL C, DLBCL D and Lung cancer. GA-R3 attains minimum value of *HS_Ratio* in case of yeast data (Cho data), Breast data A, and DLBCL B. It is important to note that GA-R2 and GA-R3 attains same value of *HS_Ratio* 48.3397 in case of Iyer data. GA-R1 and GA-R2 attains minimum value of *HS_Ratio* 2.9794 and 11.0932 for Breast data B and Breast multi data A respectively. GA-R1 and GA-R3 attains same value of *HS_Ratio* 28.2616 for Lung Cancer.

Table 7.3 contains the result obtained by FOM. HCM attains minimum value of FOM in case of Breast Multi Data A, Breast Multi Data B, DLBCL A, DLBCL D, Lung cancer and st. Jude Leukemia data. SCM attains minimum value in case of WBCD, yeast, Leukemia and Breast data B. GA-R1 attains minimum value in case of Iyer, Leukemia, DLBCL B and DLBCL C. GA-R2 attains minimum value in case of Breast data A. GA-R3 attains minimum value in case of Iris. SCM and GA-R1 attains minimum value of FOM i.e.8.7079e+006 for Leukemia data. GA-R1 and GA-R2 attains same FOM value 5.2983e+004 and 5.6860e+006 for Breast Data B and Breast multi Data A respectively. SCM and GA-R3 attains value i.e. 5.6834e+006 for Breast multi Data A.

Table 7.4 contains the result obtained by Clustering Accuracy for all fifteen datasets. Soft C-means shows superior performance in 11 cases (Iris, WBCD, Cho/yeast data, Breast data A, Breast data B, Breast Multi data A, DLBCL A, , DLBCL C, DLBCL D, Lung Cancer, St. Jude Leukemia data) over Hard C-means algorithm; while Hard C-mean shows superior performance in 4 cases (Iyer/serum, Leukemia, Breast Multi data B, DLBCL B) data over Soft C-means (Table 7.4).

GA based clustering algorithm always shows superior performance compared to Non-GA based clustering algorithm. As far as Best case analysis is concerned, GA-R3 performs better in case of Iris, WBCD, Breast data B, DLBCL A, DLBCL C; GA-R1 performs better in case of Iyer data, Breast multi data A and DLBCL B data and in rest of cases GA-R2 performs better compared to GA-R1 and GA-R3 (Table 7.4).

Table 7.3: Comparison of HCM, SCM and GA clustering algorithm using FOM (Figure Of Merit)

Sl. No.	**Datasets**	**Original**	**HCM**	**SCM**	GA-R1	GA-R2	GA-R3
1	**IRIS**	573.7335	587.4279	580.4595	586.1591	589.9501	**573.7335**
2	**WBCD**	5.4201e+003	5.3590e+003	**5.3577e+003**	5.4030e+003	5.4684e+003	5.4604e+003
3	**Iyer data/Serum data**	1.3989e+004	1.4891e+004	1.5149e+004	**1.4748e+004**	1.4763e+004	1.4763e+004
4	**Cho data (yeast data)**	8.7432e+003	8.0981e+003	**7.6874e+003**	7.9278e+003	8.0404e+003	8.3454e+003
5	**Leukemia (Golub Experiment)**	8.7050e+006	*8.7085e+006*	**8.7079e+006**	**8.7079e+006**	8.7140e+006	*8.7085e+006*
6	**Breast data A**	1.0786e+005	1.1412e+005	1.1136e+005	1.0963e+005	**1.0778e+005**	1.0970e+005
7	**Breast data B**	4.9059e+004	5.3330e+004	**5.2055e+004**	*5.2983e+004*	*5.2983e+004*	5.2091e+004
8	**Breast Multi data A**	5.6793e+006	**5.6334e+006**	*5.6834e+006*	*5.6860e+006*	*5.6860e+006*	*5.6834e+006*
9	**Breast Multi data B**	6.2678e+006	**6.2455e+006**	6.2629e+006	6.2529e+006	6.2579e+006	6.2464e+006
10	**DLBCL A**	5.4272e+005	**5.3587e+005**	5.4015e+005	5.3995e+005	5.3989e+005	5.3957e+005
11	**DLBCL B**	1.0210e+005	1.0657e+005	1.0684e+005	**1.0355e+005**	1.0445e+005	1.0476e+005
12	**DLBCL C**	3.8485e+006	3.8447e+006	3.8485e+006	**3.8406e+006**	3.8443e+006	3.8435e+006
13	**DLBCL D**	1.3557e+006	**1.2731e+006**	1.2852e+006	1.3000e+006	1.3005e+006	1.2907e+006
14	**Lung Cancer**	3.7602e+005	**3.6974e+005**	3.7198e+005	*3.7010e+005*	3.7217e+005	*3.7010e+005*
15	**St. Jude Leukemia data**	3.6193e+007	**3.6146e+007**	3.6178e+007	3.6188e+007	3.6189e+007	3.6179e+007

Table 7.4: Comparison of HCM, SCM and GA clustering algorithm using Accuracy

Sl. No.	**Datasets**	**# Samples**	**HCM**		**SCM**		**GA-R1**		**GA-R2**		**GA-R3**	
			# correct	Accuracy(%)	# correct	Accuracy(%)	# correct	Accuracy(%)	# correct	Accuracy(%)	# correct	Accuracy(%)
1	IRIS	150	133	88.67	136	90.67	140	93.33	144	96	150	**100**
2	WBCD	683	654	95.75	656	96.05	657	96.1933	661	96.7789	665	**97.3646**
3	Iyer data/Serum data	517	268	51.84	252	48.74	269	**52.0309**	266	51.4507	266	51.4507
4	Cho data (yeast data)	386	235	60.88	246	63.73	259	67.0984	287	**74.3523**	250	64.7668
5	Leukemia (Golub Experiment)	72	43	59.72	40	55.56	40	55.566	50	**69.4444**	40	55.566
6	Breast data A	98	71	72.44	86	87.75	88	89.7959	91	**92.8571**	84	85.7143
7	Breast data B	49	26	53.06	32	65.30	38	77.5510	38	77.5510	39	**79.5918**
8	Breast Multi data A	103	82	79.61	93	90.29	100	**97.0874**	100	97.0874	95	92.2330
9	Breast Multi data B	32	17	53.125	16	50	20	62.5000	23	**71.8750**	17	53.1250
10	DLBCL A	141	75	53.191	83	58.86	98	69.5035	92	65.2482	108	**76.5957**
11	DLBCL B	180	140	77.78	136	75.56	152	**84.4444**	147	81.6667	142	78.8889
12	DLBCL C	58	30	51.7241	44	75.86	46	79.3103	40	68.9655	50	**86.2069**
13	DLBCL D	129	55	42.64	65	50.38	85	65.8915	93	**72.0930**	80	62.0155
14	Lung Cancer	197	142	72.0812	150	76.14	156	79.1878	165	**83.7563**	156	79.1878
15	St. Jude Leukemia data	248	211	85.08	219	88.31	233	93.9516	235	**94.7581**	219	88.3065

7.4 Conclusion

In this chapter of the thesis, comprehensive study has been done on three cluster validation metrics (HS_Ratio, FOM and cluster Accuracy) for cluster formation algorithm (Hard C-means, soft C-means and family of GA based clustering algorithm). Given the variety of available clustering algorithms, one of the problems faced by biologists is the selection of the cluster validation metrics, which is most appropriate to a given gene expression data set. However, there is no single "best" clustering metrics which is the "*winner*" in every aspect. The performance of different clustering algorithms and different validation approaches is strongly dependent on both data distribution and application requirements. When class-labeled information are known, it is advisable to go for clustering accuracy as validation method and when class-labeled information are not known, it is advisable to go for either FOM or HS_Ratio or combination of FOM and HS_Ratio as cluster validation metrics. The choice of the clustering algorithm and validity metric is often guided by a combination of evaluation criteria and the user's experience.

Chapter 8

Conclusion

In this thesis extensive studies has been carried out on cluster formation algorithms and their application to machine learning and gene expression microarray data. Microarray data analysis is a novel topic in current biological and medical research, especially when using this technology for cancer diagnosis. Microarray data possess some important characteristic features which machine learning data do not possess. *Gene Expression Analysis* problem can be formalized as a machine learning data classification (supervised / unsupervised) problem having **high-dimension-low-sample data set** with lots of noisy/ missing data. Two set of datasets have been considered in this thesis for the simulation study. The first set contains fifteen datasets with class-labeled information and second set contains three datasets without class-labeled information. The first set of data has been used to simulate HCM, SCM and GA based clustering algorithm (chapter 4 and chapter 5). The second set of data has been used to simulate Brute-Force method and SA-HCM based clustering (chapter 6). Since the work presented in this thesis was based on un-supervised classification (i.e., clustering); class-labeled information was not used while forming clusters. In order to validate clustering algorithm, for first set of data (data with class-labeled information), clustering accuracy was used as cluster validation metric while for second set of data (data without class-labeled information), HS_Ratio was used as cluster validation metric.

The major contribution of this thesis were four-fold.

i) Comparative studies on Hard C-means and Soft C-means for machine learning data as well as Microarray cancer data: Hard C-means restricts a gene to a fixed cluster i.e., it doesn't allow a gene to participate in a more than one cluster at a time whereas a soft C-means algorithm allows soft partition of the data and allows a gene to be clustered into two or more clusters at a time with different degree of membership. Another problem with Hard C-means algorithm is that it may fall into a sub-optimal solution. A comprehensive and extensive study has been done on fifteen datasets (13 microarray gene expression data and 2 machine learning data). Since these datasets possess class-label information, clustering accuracy was used as cluster validation metric to judge the quality of cluster formed. Computer simulation shows that Soft C-means performs superior compared to Hard C-means algorithm in eleven cases out of fifteen cases. Datasets belonging to these cases are Iris, WBCD, Yeast (Cho) data, Breast Data (A, B), Multi Breast data A, DLBCL (A,C,D), Lung Cancer and St. Jude leukemia. Whereas Hard C-means shows superior performance in four cases. Datasets belonging to these cases are Serum data, Leukemia data, Breast multi data B and DLBCL B.

ii) Proposition of four different type of encoding schemes for supervised/unsupervised classification. The novelty of the algorithm lies with two factors i.e., 1) new encoding schemes and, 2) novel fitness function (HS_Ratio). Since datasets taken for studies possess class-label information, clustering accuracy was used as cluster validation metric to judge the quality of cluster formed. Extensive computer simulation shows that GA based clustering algorithm was able to provide the highest accuracy and generalization results compared to Non-GA based clustering algorithm in all cases. Average, best and worst case analysis have been done for machine learning data. As far as best case analysis is concerned, GA-R3 performs better in case of Iris, WBCD, Breast data B, DLBCL A, DLBCL C; GA-R1 performs better in case of Iyer data, Breast multi data A and DLBCL B data and in rest of cases GA-R2 performs better compared to GA-R1 and GA-R3.

iii) Proposition of Brute-Force method for cluster formation and preprocessing of data using SA for diversification for datasets without having class-labeled information: Since datasets taken for studies possess class-label information, *HS_Ratio* was used as cluster validation metric to judge the quality of cluster formed. The simulation results show that the proposed Brute-Force based Clustering approach may perform better compared to Hard C-means clustering algorithm when the no. of clusters is higher in values. Simulation result also shows that the proposed Brute-Force based Clustering approach is computationally quite faster than conventional Hard C-means clustering algorithm and thus it may be very useful when somebody deals with high dimensional microarray data. Another important feature of the proposed Brute-Force based Clustering approach in opposite to Hard C-means clustering algorithm is that; unlike Hard C-means Clustering algorithm it does not require the number of cluster i.e., the value of 'C' from user.

Simulation result also shows that the proposed approach for diversification of data using SA performs better compared to conventional Hard C-means algorithm.

iv) Comprehensive study on three cluster validation metrics (HS_Ratio, FOM and cluster Accuracy) for cluster formation algorithm (Hard C-means, soft C-means and family of GA based clustering algorithm): Given the variety of available clustering algorithms, one of the problems faced by biologists is the selection of the cluster validation metrics, which is most appropriate for a given gene expression data set. However, there is no single "best" clustering metrics which is the "winner" in every aspect. Researchers typically select a few candidate algorithms and compare the clustering results. Nevertheless, three aspects of cluster validation (i.e., quality, ground-truth and reliability) has been discussed in this thesis and for each aspect, various approaches such as HS_Ratio, Accuracy and FOM are used to assess the performance of the cluster. In fact, the performance of different clustering algorithms and different validation approaches is strongly dependent on both data distribution and application requirements. Extensive computer simulation shows that, when class-labeled information are known, it is advisable to go for clustering accuracy as validation method. When class-labeled information are unknown, in that case it is advisable to go for either FOM or HS_Ratio or combination of FOM and HS_Ratio as cluster validation metrics. The choice of the clustering algorithm and validity metric is often guided by a combination of evaluation criteria and the user's experience.

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Dissemination of Work

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Appendix A

1. Datasets without Reference data

Table 1: Snap shots of datasets without reference data (Sample Data $[10X3]$)

Sl. No.	feature 1	feature 2	feature 3
1	10	8	10
2	10	0	9
3	4	8.5	3
4	9.5	0.5	8.5
5	4.5	8.5	2.5
6	10.5	9	12
7	5	8.5	11
8	2.7	8.7	2
9	9.7	2	9
10	10.2	1	9.2

2. Datasets with Reference data(e.g.; Iris data)

Table 2: Snap Shots of Iris Data

Sl. No.	feature 1	feature 2	feature 3	feature 4	Reference Data
1	5.1	3.5	1.4	0.2	1
2	4.9	3	1.4	0.2	1
3	4.7	3.2	1.3	0.2	1
4	4.6	3.1	1.5	0.2	1
5	5	3.6	1.4	0.2	1
6	5.4	3.9	1.7	0.4	1
7	4.6	3.4	1.4	0.3	1
8	5	3.4	1.5	0.2	1
9	4.4	2.9	1.4	0.2	1
10	4.9	3.1	1.5	0.1	1
11	7	3.2	4.7	1.4	2
12	6.4	3.2	4.5	1.5	2
13	6.9	3.1	4.9	1.5	2
14	5.5	2.3	4	1.3	2
15	6.5	2.8	4.6	1.5	2
16	5.7	2.8	4.5	1.3	2
17	6.3	3.3	4.7	1.6	2
18	4.9	2.4	3.3	1	2
19	6.6	2.9	4.6	1.3	2
20	5.2	2.7	3.9	1.4	2
21	6.3	3.3	6	2.5	3
22	5.8	2.7	5.1	1.9	3
23	7.1	3	5.9	2.1	3
24	6.3	2.9	5.6	1.8	3
25	6.5	3	5.8	2.2	3
26	7.6	3	6.6	2.1	3
27	4.9	2.5	4.5	1.7	3
28	7.3	2.9	6.3	1.8	3
29	6.7	2.5	5.8	1.8	3
30	7.2	3.6	6.1	2.5	3
31	5.4	3.7	1.5	0.2	1
32	4.8	3.4	1.6	0.2	1
33	4.8	3	1.4	0.1	1
34	5	2	3.5	1	2
35	5.9	3	4.2	1.5	2

Appendix B

Reference Vector for datasets

Table 3: Iris Data

Cluster 1	Cluster 2	Cluster 3
1 to 50	51 to 100	101 to 150

Table 4: WBCD

Cluster 1	Cluster 2
1 to 444	445 to 683

Table 5: Breast A

Cluster 1	Cluster 2	Cluster 3
1 to 11	12 to 62	63 to 98

Table 6: Breast B

Cluster 1	Cluster 2	Cluster 3	Cluster 4
1 to 12	13 to 23	24 to 30	31 to 49

Table 7: Multi Breat A

Cluster 1	Cluster 2	Cluster 3	Cluster 4
1 to 26	27 to 52	53 to 80	81 to 103

Table 8: Multi Breat B

Cluster 1	Cluster 2	Cluster 3	Cluster 4
1 to 5	6 to 14	15 to 21	22 to 32

Table 9: DLBCL A

Cluster 1	Cluster 2	Cluster 3
1 to 49	50 to 99	100 to 141

Table 10: DLBCL B

Cluster 1	Cluster 2	Cluster 3
1 to 42	43 to 93	94 to 180

Table 11: DLBCL C

Cluster 1	Cluster 2	Cluster 3	Cluster 4
1 to 17	18 to 33	34 to 46	47 to 58

Table 12: DLBCL D

Cluster 1	Cluster 2	Cluster 3	Cluster 4
1 to 19	20 to 56	57 to 80	81 to 129

Table 13: Lung Cancer

Cluster 1	Cluster 2	Cluster 3	Cluster 4
1 to 139	140 to 156	157 to 177	178 to 197

Table 14: Leukemia

Cluster 1	Cluster 2
1 to 47	48 to 72

Table 15: Cho Data

Cluster 1	Cluster 2	Cluster 3	Cluster 4	Cluster 5
1 to 67	68 to 202	203 to 277	278 to 331	332 to 386

Table 16: St.JudeLeukemiaTest

Cluster 1	Cluster 2	Cluster 3	Cluster 4	Cluster 5	Cluster 5
1 to 15	16 to 42	43 to 106	107 to 126	127 to 169	170 to 248

Table 17: Iyer Data

Cluster 1	Cluster 2	Cluster 3	Cluster 4	Cluster 5	Cluster 6	Cluster 7	Cluster 8	Cluster 9	Cluster 10	Cluster 11
1 to 33	34 to 133	134 to 278	279 to 312	313 to 355	356 to 362	363 to 396	397 to 410	411 to 473	474 to 492	493 to 517

Appendix C

Result of Hard C-means Clustering Algorithm

Table 18: Iris Data

Cluster 1	Cluster 2	Cluster 3
1 to 50	51, 52, 54 to 77,79 to 100, 102 107 114 115 120 122 124 127 128 134 139 143 147 150	53, 78, 101, 104 to 106, 108 to 113, 116 to 119, 121, 123, 125, 126, 129 to 133, 135 to 138, 140 to 142, 144 to 146, 148, 149

Table 19: WBCD

Cluster 1	Cluster 2
1 3 5 to 107 109 to 134 136 to 138 140 to 151 153 to 163 165 to 181 183 to 243 245 to 444	445 447 449 to 451 453 to 462 465 to 469 471 473 474 477 to 488 491 493 to 538 540 to 567 569 to 597 601 602 604 to 625 627 to 636 638 to 683

Table 20: Breast A

Cluster 1	Cluster 2	Cluster 3
1 2 3 4 5 6 7 8 9 10 12 14 15 16 17 18 19 20 23 25 27 28 30 31 38 45 51 52 53 55 56 58 61 81	13 21 22 24 26 29 32 33 34 35 36 37 39 40 41 42 43 44 46 47 48 49 50 54 57 59 60 62 66 73 80	11 63 64 65 67 68 69 70 71 72 74 75 76 77 78 79 82 83 84 85 86 87 88 89 90 91 92 93 94 95 96 97 98

Table 21: Breast B

Cluster 1	Cluster 2	Cluster 3	Cluster 4
1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 23 26 27 29 30 31 34 35 36 41 47 49	17 28 32 39 42 43 44 48	24 25	16 18 19 20 21 22 33 37 38 40 45 4616 18 19 20 21 22 33 37 38 40 45 46

Table 22: Multi Breat A

Cluster 1	Cluster 2	Cluster 3	Cluster 4
1 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 53 54 55 56 57 58 59 60 61 62 66 70 71 72 73 74 79 80	27 28 29 30 31 32 33 34 35 36 37 39 40 41 42 43 44 45 46 47 48 49 50 51 52	63 64 65 67 68 69 75 76 77 78	2 26 38 81 82 83 84 85 86 87 88 89 90 91 92 93 94 95 96 97 98 99 100 101 102 103

Table 23: Multi Breat B

Cluster 1	Cluster 2	Cluster 3	Cluster 4
2 3 15 16 19	1 4 6 7 8 9 10 11 14 26 31 32	5 12 13 17 18 20 21 23 28 29 30	22 24 25 27

Table 24: DLBCL A

Cluster 1	Cluster 2	Cluster 3
1 2 7 11 12 13 14 19 21 23 26 28 31 32 35 36 37 38 39 40 41 42 49 51 55 57 59 60 61 62 64 65 66 67 69 70 76 92 93 94 95 97 98 108 109 115 120 121 128 130 134 135	3 4 5 6 9 10 15 16 17 18 20 22 24 25 27 29 30 33 34 43 44 45 46 47 48 50 52 54 56 58 63 68 71 72 73 74 75 77 79 80 81 82 83 84 85 86 87 88 89 90 91 96 99 101 113 118 133 136 137 138 140 141	8 53 78 100 102 103 104 105 106 107 110 111 112 114 116 117 119 122 123 124 125 126 127 129 131 132 139

Table 25: DLBCL B

Cluster 1	Cluster 2	Cluster 3
1 4 6 7 10 11 12 13 17 18 19 20 21 22 24 25 26 27 28 29 30 31 33 42 46 47 49 51 58 65 92 98 103 119 120 121 122 124 136 138 167 179	2 3 5 8 9 14 15 16 23 32 34 35 36 37 38 39 40 41 43 44 45 48 50 52 53 54 55 56 57 59 60 61 62 63 64 66 67 68 69 70 71 72 73 74 75 76 77 78 79 80 81 82 83 84 85 86 87 88 89 90 91 93 96 97 116 164	94 95 99 100 101 102 104 105 106 107 108 109 110 111 112 113 114 115 117 118 123 125 126 127 128 129 130 131 132 133 134 135 137 139 140 141 142 143 144 145 146 147 148 149 150 151 152 153 154 155 156 157 158 159 160 161 162 163 165 166 168 169 170 171 172 173 174 175 176 177 178 180

Table 26: DLBCL C

Cluster 1	Cluster 2	Cluster 3	Cluster 4
1 2 3 4 5 6 7 8 9 10 11 13 14 15 16 17 35 36 38 40 41 42 44 45	21 23 24 25 27 31 32 34 37 39 46 52 53 54 55 56 57	29 30 43 47 49	12 18 19 20 22 26 28 33 48 50 51 58

Table 27: DLBCL D

Cluster 1	Cluster 2	Cluster 3	Cluster 4
8 10 11 12 14 15 28 32 40 41 42 43 45 51 72 77 107 109 112 120	1 2 3 4 5 21 22 23 25 26 27 29 30 49 59 61 81 83 84 85 86 87 88 89 90 96 104 105	17 20 56 57 58 60 62 67 70 71 75 78 79 80 91 97 103 124	6 7 9 13 16 18 19 24 31 33 34 35 36 37 38 39 44 46 47 48 50 52 53 54 55 63 64 65 66 68 69 73 74 76 82 92 93 94 95 98 99 100 101 102 106 108 110 111 113 114 115 116 117 118 119 121 122 123 125 126 127 128 129

Table 28: Lung Cancer

Cluster 1	Cluster 2	Cluster 3	Cluster 4
2 3 4 5 6 7 8 9 10 13 16 17 22 23 25 27 28 29 31 32 34 35 36 37 38 39 40 41 43 44 45 46 47 48 49 51 52 53 54 55 56 57 58 59 60 61 62 63 64 65 66 67 70 72 73 74 75 77 80 81 82 83 84 85 87 88 91 94 95 96 98 99 100 101 102 103 106 107 108 110 116 118 119 120 121 123 124 125 127 128 129 130 131 132 133 134 136 144 157 159 160 161 162 163 165 167 168 169 174 196	15 24 26 68 79 86 90 92 111 112 113 115 117 137 139 140 141 142 143 145 146 147 148 149 150 151 152 153 154 155 156	1 11 12 14 18 19 20 21 30 33 42 50 69 71 76 78 89 93 97 104 105 109 114 122 126 135 138 158 164 166 170 171 172 173 175 176 177	178 179 180 181 182 183 184 185 186 187 188 189 190 191 192 193 194 195 197

Table 29: Leukemia

Cluster 1	Cluster 2
1 2 3 4 5 9 10 11 12 13 14 15 16 17 18 19 20 21 24 25 26 27 29 30 37 38 43 44 46 47 48 50 51 52 53 54 55 56 57 58 59 61 62 69 71	6 7 8 22 23 28 31 32 33 34 35 36 39 40 41 42 45 49 60 63 64 65 66 67 68 70 72

Table 30: Cho Data

Cluster 1	Cluster 2	Cluster 3	Cluster 4	Cluster 5
1 3 11 13 14 15 16 17 18 19 20 21 22 23 24 27 31 33 34 35 36 37 38 39 40 41 46 47 48 49 50 51 52 53 54 57 58 60 61 62 63 65 90 112 127 129 133 134 146 173 178 180 181 187 188 189 190 191 199 221 238	2 25 26 28 32 64 68 69 70 71 72 73 74 75 76 77 78 79 80 81 83 84 85 86 87 88 89 91 92 93 94 95 97 98 99 100 101 102 103 104 105 106 107 108 109 111 113 114 115 116 117 118 119 120 121 122 123 124 126 131 132 135 136 138 139 140 141 142 143 144 145 147 148 149 150 151 152 153 154 155 156 157 158 159 160 161 162 163 164 165 166 167 168 169 170 171 172 174 175 177 179 182 183 184 185 186 192 193 194 195 196 197 198 200 201 202 206 213 215 219 223 224 225 228 231 233 234 245 246 247 252 253 265 269 272 273 274 277	29 82 96 110 125 128 137 176 203 204 205 207 208 209 210 212 214 216 217 218 220 222 226 227 229 230 232 235 236 237 239 240 241 242 243 244 248 249 250 251 254 255 256 257 258 259 260 261 262 263 264 266 267 268 270 271 275 276 278 279 281 282 285 286 287 288 289 290 292 295 296 298 299 300 301 302 303 304 305 306 307 308 309 310 311 312 314 315 316 317 318 321 322 323 325 326 327 328 329 330 331 342 361	12 30 42 211 280 283 284 313 319 320 333 334 335 336 338 339 343 344 345 346 348 349 350 367 368 372 373 375 376 378 380 381 384 386	4 5 6 7 8 9 10 43 44 45 55 56 59 66 67 130 291 293 294 297 324 332 337 340 341 347 351 352 353 354 355 356 357 358 359 360 362 363 364 365 366 369 370 371 374 377 379 382 383 385

Table 31: St.JudeLeukemiaTest

Cluster 1	Cluster 2	Cluster 3	Cluster 4	Cluster 5	Cluster 6
8 12 44 45 56 69 70 75 82 88 92 170 177 178 179 184 186 188 190 191 194 196 202 210 211 213 214 217 219 220 221 224 225 229 232 233 235 239 240 241 242	16 17 18 19 20 21 22 23 24 25 26 27 28 29 30 31 32 33 34 35 36 37 38 39 40 41 42 109 110 111 112	1 3 4 5 6 7 9 10 11 13 14 15 43 46 47 48 49 50 51 52 53 54 55 57 58 59 60 62 63 64 65 66 67 68 72 73 74 76 77 78 79 80 81 83 84 85 86 87 89 90 91 93 94 95 96 97 98 100 101 102 103 104 105 106 222	2 61 71 99 107 108 113 114 115 116 117 118 119 120 121 122 123 124 125 126 131 157 168	127 128 129 130 132 133 134 135 136 137 138 139 140 141 142 143 144 145 146 147 148 149 150 151 152 153 154 155 156 158 159 160 161 162 163 164 165 166 167 169	171 172 173 174 175 176 180 181 182 183 185 187 189 192 193 195 197 198 199 200 201 203 204 205 206 207 208 209 212 215 216 218 223 226 227 228 230 231 234 236 237 238 243 244 245 246 247 248

Table 32: Iyer Data

Cluster 1	Cluster 2	Cluster 3	Cluster 4	Cluster 5	Cluster 6	Cluster 7	Cluster 8	Cluster9	Cluster10	Cluster11
20 24 25 26 32 33 365 366 373 378 379 381 383 384 387 388 389 390 391 392 393 411 413 414 415 416 424 426 429 430 431 432 433 434 437 451 453 459 460 461 462 466 467 475 476 477 479 480 481 483 485 487 495	1 2 3 4 5 10 15 17 19 34 35 36 37 39 to 107 109 to 133 141 143 144 145 146 147 156 157 161 to 181 183 184 186 to 195 197 to 216 224 225 226 227 229 231 232 242 to 249 255 258 262 263 265 266 267 268 270 271 273 274 275 277 278 283 284 285 286 287 294 295 296 297 298 299 300 301 303 328 417 499	6 7 8 9 11 12 13 14 16 18 28 134 135 136 137 138 139 140 142 148 149 150 151 152 153 154 155 158 159 160 182 185 196 217 218 219 220 221 222 223 228 230 233 234 235 236 237 238 239 240 241 250 251 252 253 254 256 257 259 260 261 264 269 272 276 315 316 317 318 319 321 322 324 326 327 329 330 331 418 421 443 474	21 23 27 38 40 108 281 282 288 289 290 291 292 293 302 304 305 306 307 308 309 310 311 312 359 478 496 497 500 502 505 512	323 336 337 338 339 340 341 344 345 346 347 350 351 399 401	279 280 356 357 358 360 361 362 494 498 503 504 506 510 511 513 514 515 516 517	22 363 364 367 368 369 371 372 374 375 376 377 380 382 385 386 394 395 396 412 427 428 436 438 439 440 457 458 469 482 484 486 488 489 490 507 508	29 30 31 313 314 320 325 332 333 334 335 342 343 348 349 352 353 354 355 397 398 400 402 403 404 405 406 407 408 409 410 419 420 422 423 444 445 447 448 449 450 452 454 455 456 463 464 465 468 493	425 435 441 446 470 492 509	442 471 472 473 491	370 501

Appendix D

Result of SCM clustering Algorithm

Table 33: Iris Data

Cluster 1	Cluster 2	Cluster 3
1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 34 18 19 20 21 22 23 24 25 26 27 28 29 30 31 32 33 34 50 35 36 37 38 39 40 41 42 43 44 45 46 47 48 49 50	52 54 55 56 57 58 59 60 61 62 63 64 65 66 67 68 69 70 71 72 73 74 75 76 77 79 80 81 82 83 84 85 86 87 88 89 90 91 92 93 94 95 96 97 98 99 100 102 107 114 120 122 124 127 128 139 143 150	51 53 78 101 103 104 105 106 108 109 110 111 112 113 115 116 117 118 119 121 123 125 126 129 130 131 132 133 134 135 136 137 138 140 141 142 144 145 146 147 148 149

Table 34: WBCD

Cluster 1	Cluster 2
1 3 5 to 107 109 to 134 136 to 138 140 to 151 153 to 163 165 to 181 183 to 243 245 to 444	445 447 449 to 451 453 to 462 465 to 469 471 473 474 477 to 488 490 to to 538 540 to 567 569 to 597 601 602 604 to 625 627 to 636 638 to 683

Table 35: Breast A

Cluster 1	Cluster 2	Cluster 3
2 9 10 20 31 38 39 46 56 66	1 3 4 5 6 7 8 12 13 14 15 16 17 18 19 21 22 23 24 25 26 27 28 29 30 32 33 34 35 36 37 40 41 42 43 44 45 47 48 49 50 51 52 53 54 55 57 58 59 60 61 62 80 81	11 63 64 65 67 68 69 70 71 72 73 74 75 76 77 78 79 82 83 84 85 86 87 88 89 90 91 92 93 94 95 96 97 98

Table 36: Breast B

Cluster 1	Cluster 2	Cluster 3	Cluster 4
1 2 3 4 5 6 7 8 9 10 11 12 49	16 18 19 20 21 22 33 37 38 40 45 46	13 14 15 24 25 26 27 28 29 30 31 35 36 41 47	17 23 32 34 39 42 43 44 48

Table 37: Multi Breat A

Cluster 1	Cluster 2	Cluster 3	Cluster 4
1 3 4 5 6 7 8 9 10 11 12 13 14 16 17 18 20 21 22 23 24 60 70	27 28 29 30 31 32 33 34 35 36 37 39 40 41 42 43 44 45 46 47 48 49 50 51 52	15 19 25 53 54 55 56 57 58 59 61 62 63 64 65 66 67 68 69 71 72 73 74 75 76 77 78 79 80	2 26 38 81 82 83 84 85 86 87 88 89 90 91 92 93 94 95 96 97 98 99 100 101 102 103

Table 38: Multi Breat B

Cluster 1	Cluster 2	Cluster 3	Cluster 4
2 3 16 19 22	6 7 8 10 11	5 12 13 14 18 20 21 23 28 29 30	1 4 9 15 17 24 25 26 27 31 32

Table 39: DLBCL A

Cluster 1	Cluster 2	Cluster 3
1 2 5 6 7 8 10 11 12 13 14 17 18 19 20 25 27 28 30 31 32 33 34 36 38 39 40 41 42 47 49 51 52 62 76 85 93 115 120 128 130 134	3 4 9 15 16 21 22 23 24 26 29 35 37 43 44 45 46 48 50 53 54 55 57 58 60 63 64 66 69 71 72 73 74 77 80 81 82 83 84 86 88 89 91 94 99 102 104 107 109 113 118 123 133 135 136 137 138 140 141	56 59 61 65 67 68 70 75 78 79 87 90 92 95 96 97 98 100 101 103 105 106 108 110 111 112 114 116 117 119 121 122 124 125 126 127 129 131 132 139

Table 40: DLBCL B

Cluster 1	Cluster 2	Cluster 3
1 3 4 5 6 7 8 9 10 11 12 13 17 18 19 20 21 22 23 24 25 26 28 29 30 31 33 38 42 43 46 47 49 51 53 58 60 64 65 66 77 79 84 91 92 98 103 119 121 122 124 136 138 167 179	2 14 15 16 27 32 34 35 36 37 39 40 41 44 45 48 50 52 54 55 56 57 59 61 62 63 67 68 69 70 71 72 73 74 75 76 78 80 81 82 83 85 86 87 88 89 90 93 94 97 120 164 175	95 96 99 100 101 102 104 105 106 107 108 109 110 111 112 113 114 115 116 117 118 123 125 126 127 128 129 130 131 132 133 134 135 137 139 140 141 142 143 144 145 146 147 148 149 150 151 152 153 154 155 156 157 158 159 160 161 162 163 165 166 168 169 170 171 172 173 174 176 177 178 180

Table 41: DLBCL C

Cluster 1	Cluster 2	Cluster 3	Cluster 4
2 3 4 5 6 7 8 11 13 14 15 16 17 35 38 40 41 42 45	12 18 19 20 22 23 25 26 28 32 33 51	1 9 10 21 24 27 31 34 36 37 39 44 46 48 52 53 54 55 56 57 58	29 30 43 47 49 50

Table 42: DLBCL D

Cluster 1	Cluster 2	Cluster 3	Cluster 4
2 3 4 5 6 8 10 11 15 16 18 22 27 28 29 30 32 45 48 49 63 81 83 84 85 86 87 89 90 96 104 105	7 9 13 19 24 26 31 33 34 35 36 37 38 39 44 46 47 50 52 53 54 55 64 65 66 68 69 76 82 92 93 94 95 98 100 108 114 117 128 129	1 17 20 21 23 25 40 41 42 43 51 56 57 58 59 60 61 62 67 70 71 72 77 78 79 80 88 91 97 112	12 14 73 74 75 99 101 102 103 106 107 109 110 111 113 115 116 118 119 120 121 122 123 124 125 126 127

Table 43: Lung Cancer

Cluster 1	Cluster 2	Cluster 3	Cluster 4
1 2 3 4 5 6 7 8 9 10 11 12 13 16 17 22 23 25 27 28 29 31 32 34 35 36 37 38 39 40 41 43 44 45 46 47 48 49 51 52 53 54 55 56 57 58 59 60 61 62 63 64 65 66 67 70 72 73 74 75 77 80 81 82 83 84 85 87 88 91 94 95 96 98 99 100 101 102 103 106 107 108 110 113 115 116 118 119 120 121 122 123 124 125 127 128 129 130 131 132 133 134 136 141 144 157 162 167 168 169 174 196	14 15 18 19 20 21 24 26 30 33 42 50 68 69 76 79 86 89 90 92 93 97 104 109 111 112 114 117 135 137 138 139 140 142 143 145 146 147 148 149 150 151 152 153 154 155 156 170 176	71 78 105 126 158 159 160 161 163 164 165 166 171 172 173 175 177	178 179 180 181 182 183 184 185 186 187 188 189 190 191 192 193 194 195 197 178 to 197

Table 44: Leukemia

Cluster 1	Cluster 2
1 2 3 4 5 9 10 11 12 13 14 15 16 17 18 20 21 24 25 26 27 29 30 37 38 43 44 46 47 48 50 51 52 53 54 55 56 57 58 59 61 69 71	6 7 8 19 22 23 28 31 32 33 34 35 36 39 40 41 42 45 49 60 62 63 64 65 66 67 68 70 72

Table 45: Cho Data

Cluster 1	Cluster 2	Cluster 3	Cluster 4	Cluster 5
1 3 4 5 7 8 9 10 11 13 14 15 16 17 18 19 20 21 22 23 24 27 29 31 33 34 35 36 37 38 39 40 41 44 46 47 48 49 50 51 52 53 54 55 57 58 59 60 61 62 63 67 90 112 127 129 130 133 134 146 181 187 188 189 190 191 199 221 238 241 293 294 299 332 347 354 359 366 370	28 68 69 70 71 72 73 74 75 76 77 78 80 81 83 84 85 87 88 91 92 93 94 95 98 99 102 103 104 106 107 108 109 111 113 114 116 117 118 120 121 122 123 124 126 135 139 140 141 142 148 149 150 151 152 153 154 155 156 157 158 159 160 161 163 164 165 166 167 169 170 171 172 175 177 179 182 192 193 195 197 215 225 228 231 246 247 269 272 273 277	2 25 26 32 64 65 79 82 86 89 96 97 100 101 105 110 115 119 125 128 131 132 136 137 138 143 144 145 147 162 168 173 174 176 178 180 183 184 185 186 194 196 198 200 201 202 204 206 208 209 213 216 219 223 224 230 232 233 234 235 240 242 244 245 252 253 264 265 266 267 271 274 275	203 205 207 210 212 214 217 218 220 222 226 227 229 236 237 239 243 248 249 250 251 254 255 256 257 258 259 260 261 262 263 268 270 276 278 279 281 282 285 286 287 288 289 290 292 295 298 300 301 302 303 304 305 306 307 308 309 310 311 312 314 315 316 317 318 323 325 326 327 328 329 330 331 342 361	6 12 30 42 43 45 56 66 211 280 283 284 291 296 297 313 319 320 321 322 324 333 334 335 336 337 338 339 340 341 343 344 345 346 348 349 350 351 352 353 355 356 357 358 360 362 363 364 365 367 368 369 371 372 373 374 375 376 377 378 379 380 381 382 383 384 385 386

Table 46: St.JudeLeukemiaTest

Cluster 1	Cluster 2	Cluster 3	Cluster 4	Cluster 5	Cluster 6
1 3 4 5 6 7 8 9 10 11 12 13 14 15 43 48 49 50 58 62 69 71 72 74 76 86 91 93 97 102 103	16 17 18 19 20 21 22 23 24 25 26 27 28 29 30 31 32 33 34 35 36 37 38 39 40 41 42 96 109 110 111 112	44 45 46 47 51 52 53 54 55 56 57 59 60 63 64 65 66 67 68 70 73 75 77 78 79 80 81 82 83 84 85 87 88 89 90 92 94 95 98 100 101 104 105 106	2 61 99 107 108 113 114 115 116 117 118 119 120 121 122 123 124 125 126 127 131 133 143 144 157 168	128 129 130 132 134 135 136 137 138 139 140 141 142 145 146 147 148 149 150 151 152 153 154 155 156 158 159 160 161 162 163 164 165 166 167 169	170 171 172 173 174 175 176 177 178 179 180 181 182 183 184 185 186 187 188 189 190 191 192 193 194 195 196 197 198 199 200 201 202 203 204 205 206 207 208 209 210 211 212 213 214 215 216 217 218 219 220 221 222 223 224 225 226 227 228 229 230 231 232 233 234 235 236 237 238 239 240 241 242 243 244 245 246 247 248

Table 47: Iyer Data

Cluster 1	Cluster 2	Cluster 3	Cluster 4	Cluster5	Cluster6	Cluster7	Cluster 8	Cluster9	Cluster10	Cluster 11
20 26 27 32 33 361 378 379 383 384 387 388 390 392 393 415 416 424 426 429 430 431 432 433 434 437 453 459 460 461 466 467 468 475 476 477 478 479 480 483 495 496 498 505 510 511 512	1 2 3 19 35 to 37 57 59 61 to 65 68 to 127 129 130 131 132 133 143 146 157 161 to 181 186 187 188 190 191 192 193 194 197 198 199 200 201 202 203 204 206 210 211 213 224 225 226 231 243 244 245 248 249 255 265 267 270 271 273 274 275 278 282 to 291 293 to 295 308 310 311 312 328 499	4 to 18 21 34 58 60 66 67 128 135 to 142 144 145 147 to 156 158 159 160 165 182 to 184 185 189 195 196 205 207 208 209 212 214 to 223 227 228 229 230 232 233 234 235 236 237 238 239 240 241 242 246 247 250 251 252 253 254 256 257 258 259 260 261 262 263 264 266 268 269 272 276 277 281 292 309 315 316 317 318 319 322 326 327 329 330 331 356 358 359 417 474 497 500 502	22 23 24 25 279 357 363 364 365 366 367 371 372 373 374 377 380 381 389 391 394 395 396 484 485 486 487 488 489 490 507 508	323 336 337 338 339 340 341 344 345 346 347 350 351 353 354 399 401 402	280 360 362 494 501 503 504 506 513 514 515 516 517	368 369 375 376 382 385 386 435 441 509	28 29 30 134 313 314 320 321 324 325 332 333 334 335 342 343 348 349 352 355 397 398 400 403 404 405 406 407 408 409 410 413 414 418 419 420 421 422 423 443 444 445 448 449 450 451 452 454 455 462 463 493	471 472	370 442 473 491	31 411 412 425 427 428 436 438 439 440 446 447 456 457 458 464 465 469 470 481 482 492

Appendix E

Data point wrongly clustered in HCM and SCM

Table 48: Data point wrongly clustered in HCM and Scm

	IRIS
K-means	FCM
53 78 102 107 114 115 120 122 124 127 128 134 139 143 147 150	53 78 102 107 114 115 120 122 124 127 128 134 139 143 147 150
	WBCD
2 4 108 135 139 152 164 182 244 446 448 452 463 464 470 472 475 476 489 490 492 539 568 598 599 600 603 626 637	2 4 108 135 139 152 164 182 244 446 448 452 463 464 470 471 472 475 476 481 489 490 492 539 568 600 603 626 637
	Breast A
11 12 14 15 16 17 18 19 20 23 25 27 28 30 31 38 45 51 52 53 55 56 58 61 66 73 80 81	13 14 15 17 23 33 37 38 40 45 46 49
	Breast B
13 14 15 16 18 19 20 21 22 23 26 27 28 29 30 31 32 34 35 36 39 41 42 43 44 47 48 49	13 14 15 17 23 33 37 38 40 45 46 49
	Multi Breast A
2 26 38 53 54 55 56 57 58 59 60 61 62 66 70 71 72 73 74 79 80	2 15 19 25 26 38 60 70 103
	Multi Breast B
1 4 5 12 13 15 16 19 23 26 28 29 30 31 32	1 4 5 9 12 13 14 15 16 17 19 22
	DLBCL A
3 4 5 6 8 9 10 15 16 17 18 20 22 24 25 27 29 30 33 34 43 44 45 46 47 48 51 53 55 57 59 60 61 62 64 65 66 67 69 70 76 78 92 93 94 95 97 98 101 108 109 113 115 118 120 121 128 130 133 134 135 136 137 138 140 141	3 4 9 15 16 21 22 23 24 26 29 35 37 43 44 45 46 48 51 52 56 59 61 62 65 67 68 70 75 76 78 79 85 87 90 92 93 95 96 97 98 102 104 107 109 113 115 118 120 123 128 130 133 134 135 136 137 138 140 141
	DLBCL B
2 3 5 8 9 14 15 16 23 32 34 35 36 37 38 39 40 41 46 47 49 51 58 65 92 96 97 98 103 116 119 120 121 122 124 136 138 164 167 179	2 14 15 16 27 32 34 35 36 37 39 40 41 43 46 47 49 51 53 58 60 64 65 66 77 79 84 91 92 94 97 98 103 119 120 121 122 124 136 138 164 167 175 179
	DLBCL C
12 18 19 20 22 26 28 29 30 33 35 36 38 40 41 42 43 44 45 47 49 57	1 9 10 12 21 24 27 29 30 31 35 38 40 41 42 43 45 48 51 52 53 54 55 56 57 58
	DLBCL D
1 2 3 4 5 6 7 9 13 16 17 18 19 20 24 28 31 32 33 34 35 36 37 38 39 40 41 42 43 44 45 46 47 48 50 51 52 53 54 55 56 59 61 63 64 65 66 68 69 72 73 74 76 77 81 83 84 85 86 87 88 89 90 91 96 97 103 104 105 107 109 112 120 124	1 7 9 12 13 14 17 19 20 21 22 23 25 27 28 29 30 32 40 41 42 43 45 48 49 51 56 63 64 65 66 68 69 73 74 75 76 81 82 83 84 85 86 87 88 89 90 91 92 93 94 95 96 97 98 100 104 105 108 112 114 117 128 129

Data point wrongly clustered in HCM and SCM

Table 49: Data point wrongly clustered in HCM and SCM

	LungCancer
1 11 12 14 15 18 19 20 21 24 26 30 33 42 50 68 69 71 76 78 79 86 89 90 92 93 97 104 105 109 111 112 113 114 115 117 122 126 135 137 138 139 144 157 159 160 161 162 163 165 167 168 169 174 196	1 11 12 14 15 18 19 20 21 24 26 30 33 42 50 68 69 71 76 78 79 86 89 90 92 93 97 104 105 109 111 112 113 114 115 117 122 126 135 137 138 139 144 157 159 160 161 162 163 165 167 168 169 174 196
	Leukemia
6 7 8 22 23 28 31 32 33 34 35 36 39 40 41 42 45 48 50 51 52 53 54 55 56 57 58 59 61 62 69 71	48 50 51 52 53 54 55 56 57 58 59 61 69 71 6 7 8 19 22 23 28 31 32 33 34 35 36 39 40 41 42 45
	Cho Data
2 4 to 10 12 25 26 28 29 30 32 42 43 44 45 55 56 59 64 66 67 82 90 96 110 112 125 127 128 129 130 133 134 137 146 173 176 178 180 181 187 188 189 190 191 199 206 211 213 215 219 221 223 224 225 228 231 233 234 238 245 246 247 252 253 265 269 272 273 274 277 278 279 281 282 285 to 312 314 to 318 321 to 331 333 334 335 336 338 339 342 to 346 348 349 350 361 367 368 372 373 375 376 378 380 381 384 386	6 12 26 28 30 32 42 43 45 56 64 65 66 79 82 86 89 90 96 97 100 101 105 110 112 115 119 125 127 128 129 130 131 132 133 134 136 137 138 143 144 145 146 147 162 168 173 174 176 178 180 181 183 184 185 186 187 188 189 190 191 194 196 198 199 200 201 202 203 205 207 210 211 212 214 215 217 218 220 221 222 225 226 227 229 231 236 237 238 239 241 243 246 247 248 249 250 251 254 255 256 257 258 259 260 261 262 263 268 269 270 272 273 276 277 280 283 284 291 293 294 296 297 299 313 319 320 321 322 324 332 347 354 359 366 370
	St.JudeLeukemia Data
1 to 7 9 10 11 13 14 15 44 45 56 61 69 70 71 75 82 88 92 99 109 to 112 170 177 178 179 184 186 188 190 191 194 196 202 210 211 213 214 217 219 220 221 222 224 225 229 232 233 235 239 240 241 242	2 43 48 49 50 58 61 62 69 71 72 74 76 86 91 93 96 97 99 102 103 109 110 111 112 127 131 133 143 144 157 168
	Iyer data
1 to 19 21 22 23 27 28 29 30 31 38 40 108 141 143 144 145 146 147 156 157 161 to 181 183 184 186 to 195 197 to 216 224 225 226 227 229 231 232 242 to 249 255 279 280 313 to 322 324 325 326 327 329 330 331 332 333 334 335 342 343 348 349 352 353 354 355 365 366 370 373 378 379 381 383 384 387 to 393 399 401 411 to 416 418 to 424 426 427 to 434 436 437 438 439 440 442 443 444 445 447 to 467 469 471 to 477 479 to 490 492 494 495 498 503 to 517	1 to 19 21 to 25 28 to 31 34 58 60 66 67 128 134 143 146 157 161 162 163 164 166 to 181 186 187 188 190 191 192 193 194 197 to 204 206 210 211 213 224 225 226 231 243 244 245 248 249 255 265 267 270 271 273 274 275 278 280 282 to 291 293 to 303 313 314 320 321 324 325 332 333 334 335 342 343 348 349 352 355 357 361 363 to 374 377 to 381 383 384 387 to 396 399 to 411 412 415 416 424 to 442 446 447 453 456 457 458 to 461 464 to 470 473 475 to 490 492 494 495 496 498 501 503 to 517

Appendix F

Data point wrongly clustered in GA based Clustering

Table 50: Data point wrongly clustered in GA based Clustering

Dataset	GA-R1	GA-R2	GA-R3
Iris	78 102 107 114 120 122 134 139 143 147	101 102 103 104 105 107	NIL
WBCD	2 4 139 244 446 448 576 577 578 579 580 581 582 583 584 585 586 587 588 589 590 591 592 593 594 600	446 448 576 577 578 579 580 581 582 583 584 585 586 587 588 589 590 591 592 593 594 600	446 448 580 581 582 583 584 585 586 587 588 589 590 591 592 593 594 600
Iyer data/Serum data	1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 21 22 23 28 29 30 31 143 146 157 161 162 163 164 166 167 168 169 170 171 172 173 174 175 176 177 178 179 180 181 186 187 188 190 191 192 193 194 197 198 199 200 201 202 203 204 206 210 211 213 224 225 226 231 243 244 245 248 249 255 265 267 270 271 273 274 275 278 280 283 284 285 286 287 294 295 296 297 298 299 300 301 303 313 314 315 316 317 318 319 320 321 322 324 325 326 327 328 329 330 331 332 333 334 335 342 343 348 349 352 355 359 365 366 367 370 373 378 379 381 383 384 387 388 389 390 391 392 393 399 401 411 412 413 414 415 416 417 418 419 420 421 422 423 424 426 427 428 429 430 431 432 433 434 436 437 438 439 440 442 443 444 445 447 448 449 450 451 452 453 454 455 456 457 458 459 460 461 462 463 464 465 466 467 468 469 473 474 475 476 477 478 479 480 481 482 483 484 485 486 487 488 489 490 492 493 494 495 496 497 498 499 500 502 503 504 505 506 507 508 509 510 511 512 513 514 515 516 517	1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 21 22 23 28 29 30 31 143 146 157 161 162 163 164 166 167 168 169 170 171 172 173 174 175 176 177 178 179 180 181 186 187 188 190 191 192 193 194 197 198 199 200 201 202 203 204 206 210 211 213 224 225 226 231 243 244 245 248 249 255 265 267 270 271 273 274 275 278 280 283 284 285 286 287 294 295 296 297 298 299 300 301 303 313 314 315 316 317 318 319 320 321 322 324 325 326 327 328 329 330 331 332 333 334 335 342 343 348 349 352 355 359 365 366 367 370 373 378 379 381 383 384 387 388 389 390 391 392 393 399 401 411 412 413 414 415 416 417 418 419 420 421 422 423 424 425 426 427 428 429 430 431 432 433 434 436 437 438 439 440 442 443 444 445 446 447 448 449 450 451 452 453 454 455 456 457 458 459 460 461 462 463 464 465 466 467 468 469 470 473 474 475 476 477 478 479 480 481 482 483 484 485 486 487 488 489 490 492 493 494 495 496 497 498 499 500 502 503 504 505 506 507 508 509 510 511 512 513 514 515 516 517	1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 21 22 23 28 29 30 31 134 135 136 137 138 139 140 141 142 143 144 145 146 147 148 149 150 151 152 153 154 155 156 157 158 159 160 161 162 163 164 165 166 167 168 169 170 171 172 173 174 175 176 177 178 179 180 181 182 183 184 185 186 187 188 189 190 191 192 193 194 195 196 197 198 199 200 201 202 203 204 205 206 207 208 209 210 211 212 213 214 215 216 217 218 219 220 221 222 223 224 225 226 227 228 229 230 231 232 233 243 246 257 261 262 263 264 266 267 268 269 270 271 272 273 274 275 276 277 278 279 280 281 286 287 288 290 291 292 293 294 297 298 299 300 301 302 303 304 306 310 311 313 324 325 326 331 343 344 345 348 349 355 365 367 370 371 373 374 375 378 280 283 284 285 286 287 294 295 296 297 298 299 300 301 303 313 314 315 316 317 318 319 320 321 322 324 325 326 327 328 329 330 331 332 333 334 335 342 343 348 349 352 355 359 365 366 367 370 373 378 379 381 383 384 387 388 389 390 391 392 393 399 401 411 412 413 414 415 416 417 418 419 420 421 422 423 424 425 426 427 428 429 430 431 432 433 434 436 437 438 439 440 442 443 444 445 446 447 448 449 450 451 452 453 454 455 456 457 458 459 460 461 462 463 464 465 466 467 468 469 470 473 474 475 476 477 478 479 480 481 482 483 484 485 486 487 488 489 490 492 493 494 495 496 497 498 499 500 502 503 504 505 506 507 508 509 510 511 512 513 514 515 516 517
Cho data (yeast data)	2 6 25 26 28 32 43 45 56 64 65 66 79 82 86 89 90 96 97 100 101 105 110 112 115 119 125 127 128 129 130 131 132 133 134 136 137 138 143 144 145 146 147 162 168 173 174 176 178 180 181 183 184 185 186 187 188 189 190 191 194 196 198 199 200 201 202 215 217 218 220 221 222 225 226 227 228 229 231 236 237 238 239 241 243 246 247 248 249 250 251 254 255 256 257 258 259 268 269 270 272 273 276 277 280 283 284 291 293 294 296 297 299 313 319 320 321 322 324 332 342 347 354 359 361 366 370	2 6 25 26 28 32 43 45 56 64 66 203 205 207 210 212 215 217 218 220 221 222 225 226 227 228 229 231 236 237 238 239 241 243 246 247 248 249 250 251 254 255 256 257 258 259 260 261 262 263 268 269 270 272 273 276 277 291 293 294 296 297 299 321 322 324 332 342 347 354 359 361 366 370	2 6 25 26 28 29 32 43 45 56 64 66 82 90 96 110 112 125 127 128 129 130 133 134 137 146 173 176 178 180 181 187 188 189 190 191 199 203 205 206 207 210 212 213 214 215 217 218 219 220 221 222 225 226 227 228 229 231 236 237 238 239 241 243 246 247 248 249 250 251 254 255 256 257 258 259 260 261 262 263 268 269 270 272 273 276 277 278 279 281 282 285 286 287 289 290 291 292 293 294 295 296 297 298 299 300 301 302 303 304 305 306 307 308 309 310 311 312 314 315 316 317 318 321 322 324 325 326 332 342 347 354 359 361 366 370

Data point wrongly clustered in GA based Clustering

Table 51: Data point wrongly clustered in GA based Clustering

Dataset	GA-R1	GA-R2	GA-R3
Leukemia (Golub Experiment)	6 7 8 22 23 28 31 32 33 34 35 36 39 40 41 42 45 48 50 51 52 53 54 55 56 57 58 59 61 62 69 71	6 7 8 22 23 28 31 32 33 34 35 36 39 40 41 42 45 48 52 53 54 69	6 7 8 19 22 23 28 31 32 33 34 35 36 39 40 41 42 45 48 50 51 52 53 54 55 56 57 58 59 61 69 71
Breast data A	11 20 31 38 39 46 56 66 80 81	11 20 31 38 46 56 80	5 6 7 8 11 20 31 38 39 46 56 67 81 82
Breast data B	29 31 35 36 41 42 43 44 47 48 49	29 31 35 36 41 42 43 44 47 48 49	17 28 31 35 36 41 42 47 48 49
Breast Multi data A	2 15 19	2 6 7 8 9 10 11 12 13 14 16 17 18 20 21 22 23 24 25 26 27 28 29 30 31 32 33 34 35 36 37 38 39 40 41 42 43 44 45 46 47 48 49 50 51 52 53 54 55 56 57 58 59 60 61 62 63 64 65 66 67 68 69 70 71 72 73 74 75 76 77 78 79 80	2 15 19 25 26 38 60 70
Breast Multi data B	1 4 5 12 13 15 16 19 17 22 23 24	1 4 5 12 13 15 16 19 30	1 4 5 12 13 16 19 23 24 27 29 30 31 32 33
DLBCL A	3 4 9 15 16 21 22 24 29 43 44 45 46 48 51 59 61 62 65 67 70 76 78 92 93 95 97 98 109 113 115 118 120 128 130 133 134 135 136 137 138 140 141	3 4 9 15 16 21 22 23 24 26 29 43 44 45 46 48 51 52 56 59 61 62 65 67 68 70 76 78 85 92 93 95 97 98 109 113 115 118 120 128 130 133 134 135 136 137 138 140 141	3 4 9 15 16 22 24 29 43 44 45 46 48 51 62 76 78 93 95 97 98 113 115 118 120 128 130 134 136 137 138 140 141
DLBCL B	2 14 15 16 32 34 35 36 37 39 40 41 46 47 49 51 58 65 92 97 103 119 121 122 124 164 167 179	2 3 5 14 15 16 32 34 35 36 37 39 40 41 46 47 49 51 58 65 77 79 92 96 97 103 119 121 122 124 164 167 179	2 3 5 14 15 16 32 34 35 36 37 39 40 41 43 46 47 49 51 53 58 60 62 64 65 77 79 92 96 97 103 119 121 122 124 164 167 179
DLBCL C	12 35 38 40 41 42 43 45 52 53 57 58	1 9 12 35 38 40 41 42 43 45 48 52 53 54 55 56 57 58	12 35 38 40 41 42 43 45
DLBCL D	20 28 30 32 40 41 42 43 45 48 51 56 63 137 138 139 140 141 142 143 144 145 146 147 148 149 150 151 152 153 154 156 160 161 164 168 170 173	1 17 20 28 32 43 45 48 51 56 63 81 82 83 84 85 86 87 88 89 90 91 92 93 94 95 96 97 98 100 104 105 108 112 114 117	1 7 9 13 14 17 19 20 28 30 32 40 41 42 43 45 48 51 56 63 64 65 66 68 81 82 83 84 85 86 87 88 89 90 91 92 93 94 95 96 97 98 100 104 105 108 112 114 117
Lung Cancer	15 18 19 20 21 24 26 33 42 50 68 69 71 76 78 79 86 89 90 92 93 97 104 105 109 111 112 114 117 126 135 137 139 144 157 162 167 168 169 174 196	15 24 26 68 71 78 79 86 89 90 92 93 97 104 105 109 111 112 114 117 126 135 137 139 144 147 152 157 158 159 164 196	15 18 19 20 21 24 26 33 42 50 68 69 71 76 78 79 86 89 90 92 93 97 104 105 109 111 112 114 117 126 144 157 162 167 168 169 174 196
St. Jude Leukemia data	2 61 69 71 99 109 110 111 112 131 133 143 144 157 168	2 61 69 71 99 109 110 111 112 131 144 157 168	2 43 48 49 50 58 61 62 69 71 72 74 76 86 91 93 96 97 99 102 103 109 110 111 112 127 131 157 168