Evolutionary Clustering Algorithm with Knowledge-Based Evaluation for Fuzzy Cluster Analysis of Gene Expression Profiles

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Abstract. Clustering method, which groups thousands of genes by their similarities of expression levels, has been used for identifying unknown functions of genes. Fuzzy clustering method that is one category of clustering assigns one sample to multiple groups according to their membership degrees. It is more appropriate than hard clustering algorithms for analyzing gene expression profiles since single gene might involve multiple genetic functions. However, general clustering methods have problems that they are sensitive to initialization and can be trapped into local optima. To solve the problems, we propose an evolutionary fuzzy clustering algorithm with knowledge-based evaluation. It uses a genetic algorithm for clustering and prior knowledge of data for evaluation. Yeast cell-cycle dataset has been used for experiments to show the usefulness of the proposed method.

1 Evolutionary Fuzzy Clustering with Knowledge-Based Evaluation

General clustering algorithms have common problems that they are very sensitive to initial values and they can be trapped by local optima since their processes are supposed to minimize objective function [1]. Besides, there is a problem of evaluating cluster results. Since gene expression profiles vary depending on their characteristics and environments that they were collected, it is not appropriate to evaluate them with the same criteria.

We propose an evolutionary fuzzy clustering and knowledge-based evaluation method to solve the problems. GA (genetic algorithm) that is an efficient method to solve optimization problem is applied for the evolutionary fuzzy clustering method. There have been many publications related to evolutionary computation for clustering. Maulik and Bandyopadhyay tried to minimize the distances between the data in the same clusters and cluster centers [1], and Hall used GA to minimize objective function value of the hard and fuzzy c-means algorithms. However, they fixed the number of clusters and used GA only for the minimization of objective function. We have encoded one cluster partition of variable number of clusters as one chromosome and formed various cluster partitions.

The proposed method is divided into two parts: an evolutionary clustering part, which searches optimal cluster partition using GA, and a knowledge-based evaluation part, which obtains the optimal α -cuts from several datasets for Bayesian validation (BV) method. Fuzzy c-means algorithm known as the most widely used fuzzy clustering method is used for clustering [2].

For knowledge-based evaluation, we have used BV and decision tree (DT) rule to decide the optimal α -cut value. Original BV [3] evaluates cluster partition with the same α -cuts for all datasets, but it cannot evaluate the cluster results correctly since each dataset has different distribution and they are extracted from different environments.

We have obtained α -cut value for each dataset using the DT rule. First, N gene expression profiles are clustered using the fuzzy c-means algorithm, and the results are evaluated by BV. Subsequently, the optimal α -cut for each dataset is decided, and they are used for the labels of DT training data. Rule production process trains DT, and produces rules. As Fig. 1 illustrates, the attributes of DT training data are produced using membership matrices that are the fuzzy clustering results of each dataset. Incrementing the membership degree value from 0.0 to 1.0 with the difference of 0.1, attributes are divided into 10 sections. Each section counts the frequency of samples and calculates the attribute by dividing the frequency by the total number of samples. These attributes calculated are $A_1 \sim A_{10}$.

Fig. 1. Training data production process of decision tree

Fig. 2. Representation of variable length chromosome

The training process sets α -cut value when experimental dataset is inputted. Using these α -cut values, BV calculates the final Bayesian score (BS), which is the degree of fitness evaluation.

For evolutionary clustering, we have used floating point representation to represent a set of cluster centers of cluster partition. One cluster partition contains K clusters, and a chromosome is represented in a space of $N \times K$ in case that the dimension of each center is N . Fig. 2 illustrates several chromosomes that are in one cluster partition, and each chromosome can have different number of clusters and different values of cluster centers.

Population is initialized at random. The cluster numbers less than square value of the sample size have been used for clustering. The minimum number of clusters is set as 2. To evaluate fitness, all samples are clustered using fuzzy c-means algorithm, first. After cluster centers are updated, the chromosomes with updated centers are evaluated by BV. A roulette wheel strategy is used for selection. Crossover and mutation operations are performed considering variable length chromosomes.

2 Experiments and Analyses

We have performed experiments with yeast cell-cycle dataset, and it has expression levels of 6000 genes expressed during two cell cycles. 421 genes that show significant change of expression levels are used here, referring related work [4].

Maximum generation number of 1000 and population size of 200 have been used for experiments. Maximum numbers of clusters have been set by 20, and crossover rate of 0.8 and mutation rate of 0.01 have been used. The fuzziness parameter of the fuzzy c-means algorithm has been set as 1.2.

α -cut value of yeast cell-cycle dataset is decided as 0.4 by DT. Table 1 shows the training data extracted from yeast cell-cycle and SRBCT datasets. Comparing SRBCT, Values in A_2 and A_9 of yeast cell-cycle dataset are larger, and the value in A_{10} is smaller because the samples of yeast cell-cycle dataset have fuzzier cluster boundaries than SRBCT dataset. This shows that the characteristics of dataset should be considered since they are different.

Table 1. Training data of DT

Dataset	Attributes of training data									
	A_1	A_2	A_3	A_4	A_5	A_6	A_7	A_8	A_9	A_{10}
Yeast	1.000	0.231	0.114	0.086	0.071	0.064	0.059	0.069	0.162	0.546
SRBCT	1.000	0.016	0.000	0.016	0.000	0.016	0.000	0.000	0.048	0.937

We have compared the proposed method with the original FCM by means of BS and the objective function value (OF value) of the FCM. Table 2 shows 10 experimental results of yeast cell-cycle dataset. If BS is high and the objective function value is low, it means that clustering is performed well since the objective function value is based on the distances between cluster centers and samples. The proposed method shows better results than original FCM in both BS and OF value.

Table 2. Comparison experiments of original FCM and GA+FCM

Count	Original FCM		GA+FCM	
	BS	OF value	BS	OF value
1	0.03354	164.472	0.13256	166.883
2	0.00875	163.670	0.11246	161.542
3	0.03238	165.057	0.12661	162.911
4	0.03825	162.653	0.08058	162.073
5	0.02165	163.758	0.10667	162.798
6	0.04096	164.086	0.09778	162.312
7	0.02806	163.052	0.11873	162.042
8	0.04473	164.877	0.13659	162.773
9	0.02478	162.452	0.12898	162.905
10	0.04645	169.216	0.11246	161.542
Average	0.03195	164.329	0.11534	162.778

Finally, we have compared and analyzed the experimental result with the known genes of Cho's work [4]. We have focused on fuzzy genes that belong to several clusters at the same time with the membership degrees higher than 0.3. Fig. 3 illustrates the gene description and cluster number of fuzzy genes.

Fig. 3. Gene description and cluster number of fuzzy genes

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