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Neural Network Based Virtual Reality Spaces for Visual Data Mining of Cancer Data: An Unsupervised Perspective

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Abstract. Three microarray gene expression cancer databases are represented using neural networks and visual data mining with virtual reality spaces. The databases contains data from cancerous and noncancerous tissues. In order to understand the structure of the data, structure-preserving virtual spaces are constructed using Samann neural networks. High quality visual representations are obtained. For the databases under study, the virtual spaces are clearly polarized with two distribution modes, each one corresponding to a different class.

1 Introduction

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2 Neural Networks for the Construction of Virtual Reality Spaces

Virtual reality spaces for the visual representation of information systems [1, 2] were introduced in [3]. The typical *desiderata* for the visual representation of data and knowledge can be formulated in terms of minimizing information loss, maximizing structure preservation, maximizing class separability, or their combination, which leads to single or multi-objective optimization problems. In many cases, these concepts can be expressed deterministically using continuous functions with well defined partial derivatives. This is the realm of classical optimization where there is a plethora of methods with well known properties. In the case of heterogeneous information the situation is more complex and other techniques are required [4].

In the unsupervised case, the function f mapping the original space to the virtual reality (geometric) space \mathbb{R}^m can be constructed as to maximize some metric/non-metric structure preservation criteria as is typical in multidimensional scaling [5], or minimize some error measure of information loss [6]. A typical error measure is:

$$Sammon\ Error = \frac{1}{\sum_{i < j} \delta_{ij}} \sum_{i < j} \frac{(\delta_{ij} - \zeta_{ij})^2}{\delta_{ij}} \quad (1)$$

where δ_{ij} is a dissimilarity measure between any two objects i, j in the original space, and ζ_{i^v, j^v} is another dissimilarity measure defined on objects i^v, j^v of the virtual reality space (the images of i, j under f). Usually, the mappings f obtained using approaches of this kind are *implicit* because the images of the objects in the new space are computed directly. However, a functional representation of f can be obtained with neural networks: the Samann network. This is a feedforward network and its architecture consists of an input layer with as many neurons as descriptor attributes, an output layer with as many neurons as the dimension of the virtual reality space and one or more hidden layers. The classical way of training the Samann network is described in [7].

3 Cancer Data Sets Description

We selected three microarray gene expression cancer databases related to three of the leading causes of cancer death in the world.

3.1 Gastric Cancer Data

A study of genes that are differentially expressed in cancerous and noncancerous human gastric tissues was performed in [8]. The original database contained 30 samples (22 tumor, 8 normal) that were analyzed by oligonucleotide microarray, obtaining the expression profiles for 6936 genes (7129 attributes). Using the 6272 genes that passed a prefilter procedure, cancerous and noncancerous tissues were successfully distinguished with a two-dimensional hierarchical clustering using Pearson's correlation. However, the clustering results used most of the genes on the array. To identify the genes that were differentially expressed between cancer and noncancerous tissues, a Mann-Whitney's U test was applied to the data. As a results of this analysis, 162 and 129 genes showed a higher expression in cancerous and noncancerous tissues, respectively. In addition, several genes associated with lymph node metastasis and histological classification (intestinal, diffuse) were identified.

3.2 Lung Cancer Data

Gene expressions were compared in [9] for severely emphysematous lung tissue (from smokers at lung volume reduction surgery) and normal or mildly emphysematous lung tissue (from smokers undergoing resection of pulmonary nodules).

The original database contained 30 samples (18 severe emphysema, 12 mild or no emphysema), with 22283 attributes. Genes with large detection P -values were filtered out, leading to a data set with 9336 genes, that were used for the subsequent analysis. Nine classification algorithms were used to identify a group of genes whose expression in the lung distinguished severe emphysema from mild or no emphysema. First, model selection was performed for every algorithm by leave-one-out cross-validation, and the gene list corresponding to the best model was saved. The 102 genes reported by at least four classification algorithms were chosen for further analysis. With these genes, a two-dimensional hierarchical clustering using Pearson's correlation was performed that distinguished between severe emphysema and mild or no emphysema. Other genes were also identified that may be causally involved in the pathogenesis of the emphysema.

3.3 Liver Cancer Data

Zebrafish liver tumors were analyzed and compared with human liver tumors in [10]. First, liver tumors in zebrafish were generated by treating them with carcinogens. Then, the expression profiles of zebrafish liver tumors were compared with those of zebrafish normal liver tissues using a Wilcoxon rank-sum test. The original database had 20 samples (10 normal, 10 tumor) and 16512 attributes. As a result of this comparison, a zebrafish liver tumor differentially expressed gene set consisting of 2315 gene features was obtained. This data set was used for the comparison with human tumors. The results suggest that the molecular similarities between zebrafish and human liver tumors are greater than the molecular similarities between other types of tumors (gastric, lung and prostate).

4 Experiments

4.1 Experimental Setting

Data sets. We tested the aforementioned original microarray gene expression databases for gastric [8] (7129 attributes, 22 tumor and 8 normal samples), lung [9] (22283 attributes, 18 severe emphysema and 12 mild or no emphysema samples) and liver cancer [10] (16512 attributes, 10 normal and 10 tumor samples). These databases can be found at ???no se si son publicas???

Data preprocessing. For gastric and lung data, each gene was scaled to mean zero and standard deviation one (original data were not normalized). For liver data, no transformation was performed (original data were \log_2 ratios).

Model training. For every data set, Samann networks were constructed to map the original data to a 3-D virtual reality space. The activation functions used were sinusoidal for the first hidden layer and hyperbolic tangent for the rest. A collection of models was obtained by varying some of the network controlling parameters (number of units and weights range in the first hidden layer,

	Sammon Error			
Data Set	Minimum	Maximum	Mean	Std.Dev.
Gastric Cancer	0.062950	0.077452	0.072862	0.003346
Lung Cancer	0.079242	0.107842	0.094693	0.006978
Liver Cancer	0.039905	0.055640	0.049857	0.003621

Table 1. Statistics of the best 1000 Samann networks obtained.

learning rates, momentum, number of iterations, random seeds), for a total of 1944 Samann networks for every data set.

Computing environment. All of the experiments were conducted on a Condor pool (<http://www.cs.wisc.edu/condor/>) located at the Institute for Information Technology, National Research Council Canada.

4.2 Results

The distributions of the Sammon error showed a good behavior, since it was skewed towards the smallest errors and fluctuating within a narrow range. In table 1 some statistics of the experiments can be found: minimum, maximum, mean and standard deviation for the best (i.e., with smallest Sammon error) 1000 networks.

Clearly, it is impossible to represent a virtual reality space on printed media (navigation, interaction, and world changes are all lost). Therefore, only snapshots can be presented. Figures 1, 2 and 3 show the virtual reality spaces corresponding to the best networks for the gastric, lung and liver cancer data sets respectively. Although the mapping was generated from an unsupervised perspective (i.e., without looking at the class labels), points of every class were labelled *a posteriori*. Transparent membranes wrap the corresponding classes.

The low value of the Sammon error indicates that the spaces preserved most of the distance structure of the data, therefore, giving a good idea about the distribution in the original spaces. The three virtual spaces are clearly polarized with two distribution modes, each one corresponding to a different class. Note, however, that classes are more clearly differentiated for the liver and gastric data sets than for the lung data set, where a certain level of overlapping exists. In this case, data seems to be placed in a spherical surface, with classes roughly separated by a hyperplane (in the virtual space).

The advantage of using Samann networks is that, since the mapping f between the original and the virtual space is *explicit*, a new sample can be easily transformed and visualized in the virtual space. Since the distance between any two objects is an indication of their dissimilarity, the new point is more likely to belong to the same class of its nearest neighbors. This helps *la toma de decisiones* and avoids numerical computations from scratch (clustering or classification procedures, see section 3)

5 Conclusions

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Acknowledgments

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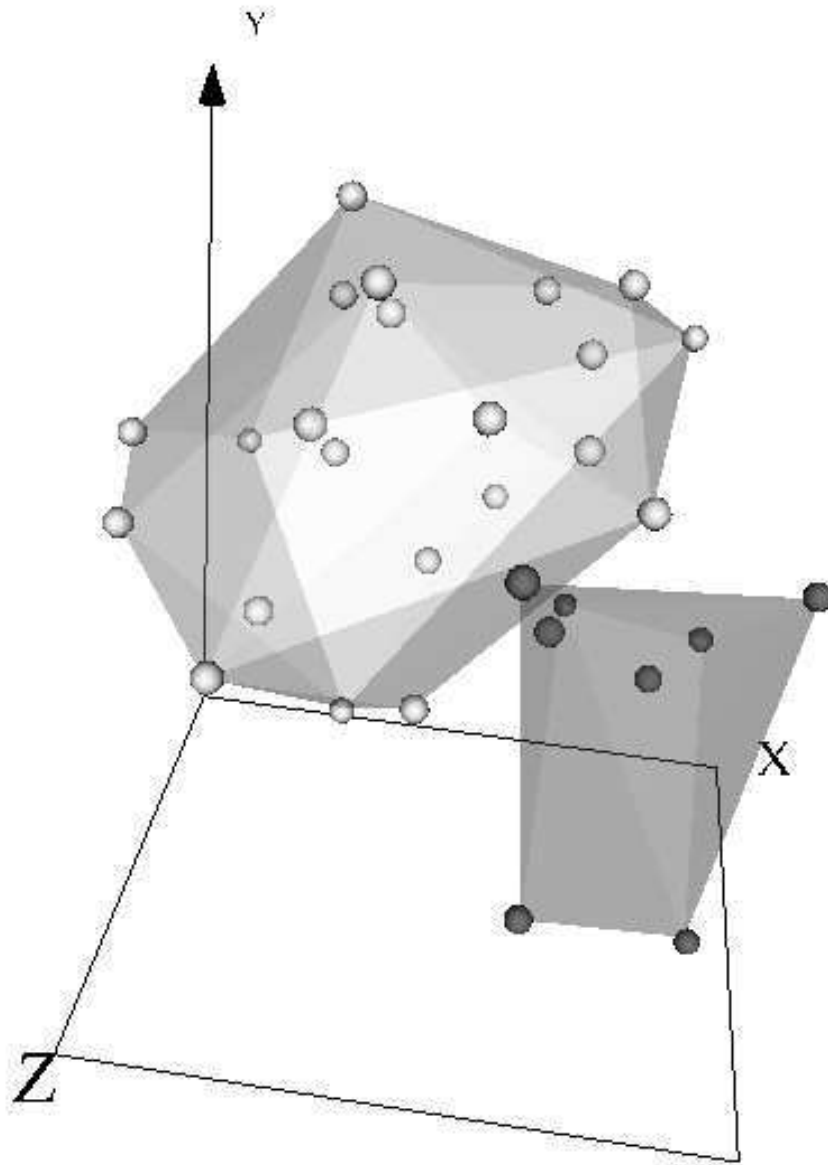


Fig. 1. Virtual reality space of the gastric cancer data set (Sammon error = 0.063). Dark and light spheres are noncancerous and cancerous samples, respectively. Transparent membranes wrap the corresponding classes.

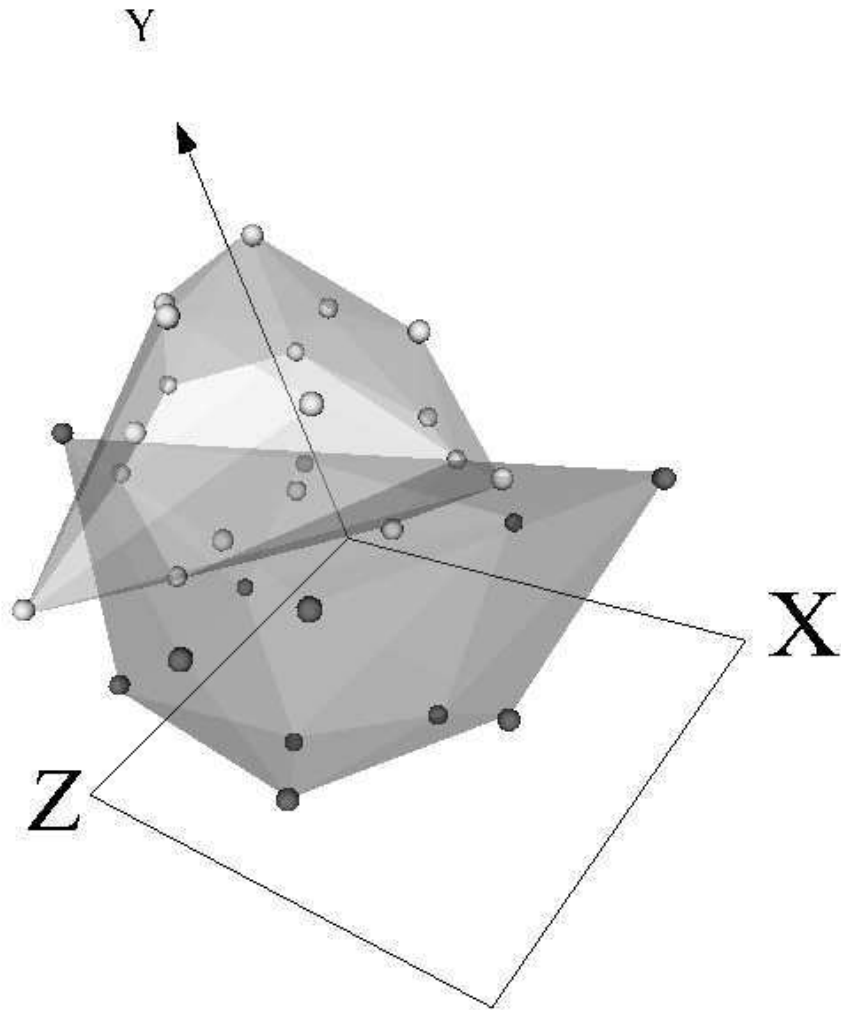


Fig. 2. Virtual reality space of the lung cancer data set (Sammon error = 0.079). Dark and light spheres are severe emphysema and no or mild emphysema, respectively. Transparent membranes wrap the corresponding classes.

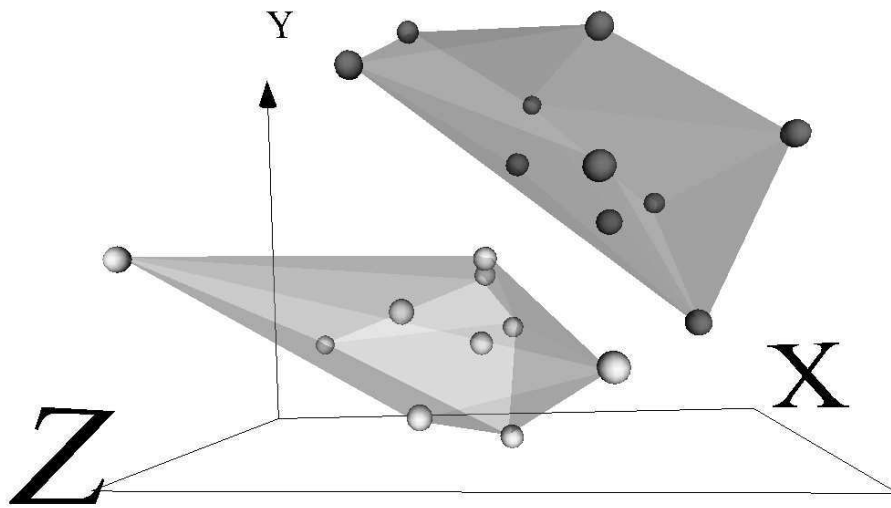


Fig. 3. Virtual reality space of the liver cancer data set (Sammon error = 0.040). Dark and light spheres are normal and tumor samples, respectively. Transparent membranes wrap the corresponding classes.