Algorithm for Finding Optimal Gene Sets in Microarray Prediction

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February 9, 2008

Abstract

Motivation: Microarray data has been recently been shown to be efficacious in distinguishing closely related cell types that often appear in the diagnosis of cancer. It is useful to determine the minimum number of genes needed to do such a diagnosis both for clinical use and to determine the importance of specific genes for cancer. Here a replication algorithm is used for this purpose. It evolves an ensemble of predictors, all using different combinations of genes to generate a set of optimal predictors.

Results: We apply this method to the leukemia data of the Whitehead/MIT group that attempts to differentially diagnose two kinds of leukemia, and also to data of Khan et. al. to distinguish four different kinds of childhood cancers. In the latter case we were able to reduce the number of genes needed from 96 down to 15, while at the same time being able to perfectly classify all of their test data.

Availability: [http://stravinsky.ucsc.edu/josh/gesses/](http://stravinsky.ucsc.edu/josh/gesses/)

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Introduction

cDNA microarrays have been used with great success to distinguish cell types from each other, and hence has promising applications to cancer diagnosis. While the histopathology of two cells may appear very similar, their clinical behavior, such as their response to drugs can be drastically different. The use of microarrays has been shown in many cases to provide clear differential diagnosis rivaling or surpassing other methods and leads to a clustering of data into different forms of a disease (DeRisi et al., 1996; Alon et al., 1999; Perou et al., 1999; Zhu et al., 1998; Wang et al., 1999; Schummer et al., 1999; Zhang et al., 1997; Alizadeh et al., 2000; Golub et al., 1999; Khan et al., 2001).

Many approaches have been used to classify microarray data. These include the use of artificial neural networks (Khan et al., 2001; Furey et al., 2000), logistic regression (Li & Yang, 2001), support vector machines (Brown et al., 2000; Furey et al., 2000), coupled two-way clustering (Getz et al., 2000), and weighted votes - neighborhood analysis (Golub et al., 1999). For much of the data all these techniques appear to give similar results and their performance improves as the amount and quality of data increases. For example work on the classification of two different leukemias (Golub et al., 1999) attempts to classify 34 test samples based on 38 training samples. On prediction of test data, different predictors make anywhere from 0 to 5 mistakes. On the other hand, recent work on small round blue cell tumors (SRBCT) attempted to classify 20 test samples based on 63 training samples (Khan et al., 2001). They were able to classify all test data correctly into one of four separate categories. They were able to do this with a single layer neural network that considered only 96 genes.

To classify samples using microarray data, it is necessary to decide which genes should be included in a predictor. Including too few genes will not discriminate in a detailed enough manner to classify test data correctly. Having too many genes is not optimal either, as many of the genes are largely irrelevant to the diagnosis and mostly have the effect of adding noise, decreasing the “information criterion” (Li & Yang, 2001; Akaike, 1974; KP Burnham, 1998; Schwarz, 1976). This is particularly severe with a noisy data set and few subjects. Therefore an effort is made to choose an optimal set of genes for which to start the training of a predictor. This is done in a variety of different ways, such as a kind of neighborhood analysis (Golub et al., 1999), principle component analysis (Khan et al., 2001), or gene shaving (Hastie et al., 2000). A predictor can then be developed from this carefully chosen subset of genes.

Recent work (Li & Yang, 2001) addressed the problem of gene selection for a leukemia data set (Golub et al., 1999). They initially ranked genes as had been done in the first analysis (Golub et al., 1999) and used the top ranked genes. They varied the number they included and found no clear indication of any optimum number aside from the conclusion that the number should be much smaller than the 50 that had been originally used (Golub et al., 1999).

Here we develop gene selection further by making it an integral part of the prediction algorithm itself. Instead of using all of the highest ranked genes, we find an effective method to greatly reduce this number. This can be done because gene expression tends to be highly correlated, making many of the
initially chosen genes redundant or even deleterious because of the problem of added noise.

The method introduced here is named GESSES (genetic evolution of sub-sets of expressed sequences). It makes use of a kind of evolutionary algorithm known as a replication algorithm that has been extensively used in quantum simulations (Ceperley & Kalos, 1979) and protein folding (Garel & Orland, 1990). It finds a set of highly relevant genes by considering a whole ensemble of predictors, each of which use a different sets of genes. As the predictors evolve, more genes are added to each predictor. It eventually produces an ensemble of predictors each of which can be tried on test data.

In the case of small round blue cell tumors, GESSES reduces the number of genes from 96 down to below 15 while still predicting the test data perfectly.

Aside from optimizing predictive capabilities, it is hoped that GESSES will have applications in the clinical diagnosis of cancer (He & Friend, 2001). For this purpose it is important to use as few genes as possible and still obtain an accurate diagnosis of the disease.

With the same algorithms applied to leukemia data of Golub et. al., we find conclusions in accord with Li and Yang (Li & Yang, 2001) that there is no clear indication of an optimum number of genes to use in a predictor. We find a range of predictors some that predict the test data perfectly but many predictors that get several samples wrong. This is also in accord with other groups work (Golub et al., 1999; Furey et al., 2000). Without further data or further biological information, it is probably not possible to do better than this. This paper is organized as follows. We discuss the algorithm used in detail by first defining the terminology and concepts used. Then we discuss the predictor used, the kind of evolutionary algorithms and the scoring function. We then apply this to two data sets, the SRBCT and leukemia data. Last, we make some concluding remarks.

The Algorithm

Terminology

We have samples of microarray training data \( D_t \equiv \{ D_1, D_2, \ldots \} \) with each sample consisting of \( N \) genes. Corresponding to the \( i \)th gene of a sample is its expression level \( e_i \). The complete set of genes \( \mathcal{G}_t \) is the collection of genes 1 through \( N \) and we will consider subsets of \( \mathcal{G}_t \), for example the subset \( \mathcal{G}_t \equiv \{ \alpha_1, \alpha_2, \ldots, \alpha_m \} \) (e.g. genes 2,5, and 9), which we denote \( \mathcal{G}_\alpha \). For this subspace of genes the vector of expression levels \( e_\alpha \equiv (e_{\alpha_1}, \ldots, e_{\alpha_m}) \). The number \( m \) of genes in this subset is denoted \( |\alpha| \), which in this case is \( m \).

Each sample \( D \) has a classification of type \( T \), in this case the type of cancer, which can take one of \( N_T \) values. The set of possible types is denoted \( T \).

We introduce the usual definition of the Euclidean distance between samples \( D_a \) and \( D_b \) on the subspace \( G_\alpha \):

\[
\begin{align*}
\bar{d}^2(a,b) = \frac{1}{|\alpha|} \|e_\alpha^a - e_\alpha^b\|^2 = \frac{1}{|\alpha|} \sum_{i=1}^{|\alpha|} |e_{\alpha_i}^a - e_{\alpha_i}^b|^2
\end{align*}
\]

(1)
where $e^a_\alpha$ and $e^b_\alpha$ are the expression levels of samples $a$ and $b$ respectively, for genes $\alpha_1, \alpha_2, \ldots, \alpha_m$.

**Predictor**

We define a predictor $P$ as a function that takes a data sample $D$ and outputs a type $T$, in this case the type of cancer that is associated with that data. That is $P(D) \rightarrow T$.

In this work we will use a k-nearest neighbor search (Duda & Hart, 1973) to construct the predictor. In the results reported below, we use $k = 1$, that is, the set of samples that forms the training data $D_t$ are compared with the target sample $D$ by finding the distance using eqn. (1) between $D$ and each vector in the training set. The sample in the training set closest to $D$ gives the classification $T$ of $D$. The distance depends on what subspace of genes $G$ is used hence the predictor depends both on the training data and $G$. Sometimes we will explicitly denote this dependence by writing the predictor as $P_G$.

We will use variants of this basic predictor when constructing a scoring function that we discuss below. For this we will not only need the closest point, but the values of the distances to all sample points.

**Evolution Algorithms**

Starting off with an ensemble of different gene subspaces we want to determine rules to evolve it to a new one that gives a better set of predictors. To do this, we have to have a measure of how well a predictor classifies samples into separate types. We do this by means of a scoring function.

**Scoring function**

The scoring function is used to determine how well the predictor predicts data. By definition we cannot use any information from the independent test data in the development of the predictors. Therefore we consider only the training data $D_t$ to determine the fitness of a predictor. In other words, we need to score the effectiveness of the predictor using only $D_t$. This is done as follows.

1. We consider one point $D_p$ in $D_t$ as a pseudo test data point, and eliminate this point from $D_t$, calling the resultant training data $D'_t$. We then loop over all points in $D_p \in D_t$ in the following steps.

   (a) We find the set of distances between $D_p$ and points in $D'_t$.

   (b) If the type of the point giving the shortest distance matches the type of $D_p$, we add 1 to the scoring function. Otherwise we add nothing and skip the remaining steps, continuing to loop over the remaining $D_p$’s.

   (c) We consider the distances grouped by the classification type of the target points. We consider the shortest distance of each type from $D_p$, which we call $d_1, d_2, \ldots, d_{N_T}$.
(d) Of these we take the two shortest, $d_i$ and $d_j$ and add $C|d_i^2 - d_j^2|$ where $C$ is a constant chosen so that the value of this added term is $\ll 1$.

The scoring function depends on the predictor, which in turn is determined by the training data and the subspace of genes $G$. We will denote this latter dependence as $S_G$.

**Initial Gene Pool**

Often it is necessary to narrow down the genes that are considered from the many thousand that are measured on the microarray down to of order $10^2$ that are most relevant. There are many ways of doing this, one common method being principle component analysis. For the purposes here we choose instead a different method that is highly effective.

We consider how genes distinguish two types $t_1, t_2 \in T$ from each other. For each gene $g \in \mathcal{G}_i$ we consider its expression levels in the training samples. We rank all the training samples in terms of the expression level of $g$. We are looking for genes that for high levels give type $t_1$ and for low levels give type $t_2$ (or vice-versa). When ranked this way, they sometimes will perfectly separate, that is the first part of the list is one type, and the last part is the other. These genes are ranked the highest. Most of the time however, a gene will not separate so clearly and there will be overlapping regions. Those with more overlaps of different types are ranked lower. In this way we have a ranking of the genes that are best able to distinguish $t_1$ from $t_2$, and we pick the top $M$ genes.

We then consider all distinct combinations of $t_1$ and $t_2$ and pick the best $M$ genes from each combination. Genes may overlap, narrowing the initial pool. This is our initial set of genes $\mathcal{G}_i$ that we will consider.

**Statistical Replication**

In analogy with statistical mechanics, we can think of the scoring function as (negative) energy and invent a dynamics that evolves them towards the highest scoring (lowest energy) states. We do this at finite temperature to allow the system to accept predictors that occasionally may be less fit than their predecessors to get rid of local minima in predictor space and to allow for a diverse population of predictors.

Suppose the system has evolved to an ensemble of $n$ gene subspaces $\mathcal{E} \equiv \{G_1, G_2, \ldots, G_n\}$, we will now employ a variant of a replication algorithm used in other contexts ([Ceperley & Kalos, 1979]) to replicate and modify each of the $G_i$’s.

1. For each $G \in \mathcal{E}$ we produce a new subspace as follows.
   (a) A set of genes $G$ has genes $\{g_1, g_2, \ldots, g_m\}$. We randomly choose a gene $g_r$ from the initial set $\mathcal{G}_i$, and add it to $G$, producing a new set $G'$ of genes $\{g_1, g_2, \ldots, g_m, g_r\}$. If $g_r \in G$, $G' = G$.
   (b) We compute the difference in the scoring functions $\delta S = S_{G'} - S_G$. 

(c) We compute the weight for $G'$, $w = \exp(\beta \delta S)$, where $\beta$ is the inverse “temperature”.

2. Let $Z$ denote the sum of these weights. We normalize the weights by multiplying them by $n/Z$.

3. We replicate all subspaces according to their weights. With a weight $w$, the subspace is replicated $\lfloor w \rfloor$ and an additional time with probability $w - \lfloor w \rfloor$. Here $\lfloor w \rfloor$ denotes the largest integer $< w$.

In summary, every subspace in the system is mutated and replicated in accordance with how much fitter it was than its predecessor. By carefully normalizing the system, the number of subspaces in the ensemble stays close to $m$. Note that we can also do more than one potential mutation in step 1. We will generalize this to allow $n_m$ potential mutations.

**Annealing**

As the system evolves, the scoring function gives similar answers for all members of the ensemble. In order to improve convergence, it is useful to make the temperature a function of the spread in scores (or energy). A variety of schedules for the temperature were tested. We have found that good results are obtained if $\beta$ is taken to be $2/\Delta E$, where $\Delta E$ is the maximum spread in scores between different members of the ensemble.

This is particularly useful because the scoring function has two basic components. The first adds unity every time a sample is correctly classified. The second adds a much smaller number proportional to the constant $C$ defined above, which is chosen to make this second component $\ll 1$. The second component tries to maximize the separation between the different classes. When the predictors have evolved so that they are all classifying correctly, we would like the second part to take effect. By lowering the temperature by a schedule such as the one above, the algorithm will then select for predictors that maximize the second part of the scoring function. This leads to a much better set of genes.

**Deterministic Evolution**

As an alternative to the statistical replication method above, we also employed a method that is computationally more expensive but that often performs better. The statistical method does not explore all possible combinations of genes at each stage of growth. This can miss optimal gene combinations. We get around this by a deterministic exploration of the optimum gene combinations at every step. A single step goes as follows:

1. Construct all distinct unions of the $G$'s in the ensemble $E$ with individual genes in the initial gene pool $G_i$, i.e. $g_1, g_2, \ldots, g_m, g_i$.

2. Sort all of these combinations by their score, keeping the top $n_{\text{top}}$ of them.

To save computer time we tried various values for $n_{\text{top}}$. It was found that $n_{\text{top}} = n$, (the number of $G$'s in the ensemble) performed quite well. Another variant was to construct only half the unions and keep the top $n$, for computational efficiency.
Results

We now discuss application of the above algorithm to two data sets. The work on the small round blue cell tumors (SRBCT) of childhood and the work on human acute leukemia (Golub et al., 1999).

SRBCT Data

Small round blue cell tumors (SRBCT) of childhood are hard to classify by current clinical techniques. They appear similar under a light microscope and several techniques are normally needed to obtain an accurate diagnosis. The paper (Khan et al., 2001) used microarrays to study their classification using of a single layer neural network. This work differed from previous studies in that they were attempting to distinguish between four different cancer types instead of the more usual 2. They used 63 samples for training and tested with 20. By using a clever method combining principle component analysis and sensitivity of their neural network to a gene, they were able to reduce the number genes needed to 96 yet still classify all different forms of cancer in test data perfectly.

Here we use the same data set to reduce the number of genes needed and still classify the test data perfectly.

Starting with their data set of 2308 genes, we constructed the initial pool of genes by considering how well a gene discriminates type $i$ cancer from type $j$, as described above. Since there are 4 possible types, we have 6 combinations of $i$ and $j$. For each of these we take the top 10 genes best able to discriminate for each $i, j$ pair. This gives a total of 50 genes, because it turns out that 10 of these overlap between groups.

We then evolve these gene subspaces according to the statistical replication method described above. Fig. 1 shows the average number of genes in a predictor as a function of the number of generations. The average is over the ensemble of predictors. It starts to level off significantly at the 38th generation, because the addition of further genes does not improve the scoring. Fig. 2 shows how as a function of the average number of genes, the predictors fair with the test data of 20 samples. The vertical axis is the average number of incorrect assignments, again averaged over all predictors in the ensemble. By the 26th generation, more than 90% of predictors perform perfectly with the test data, and by the 41st generation, all predictors perform perfectly using an average of 28 genes.

We next use the deterministic evolution method described above only constructing half the unions. Fig. 3 shows the average number of genes in a predictor as a function of the number of generations. In this case it plateaus off sooner, after about 15 generations. The comparison with the test data is shown in Fig. 4. Here all predictors perform perfectly when the average number of genes in a predictor is 15.1. Here we only used half the possible unions and kept $n_{\text{top}} = 50$.

Encouraged by the above results we did a larger run starting with an initial pool of 90 genes of which 15 overlapped, giving a total of 75 initial genes. Evolving these with $n_{\text{top}} = 150$ gives the results shown in fig. 5. Of the top 100 predictors, all predicted the test data perfectly. The average number of genes
in a predictor was 12.7.

With this data, GESSES can be used to give an ensemble of predictors that have perfect or near perfect performance. However if the initial gene pool is reduced to below 60 genes, it degrades. For example, starting with the top 48 genes (giving 41 distinct genes) with $n_{top} = 41$ leads to a set of predictors that make an average of 0.439 mistakes, and an average number of genes of 11.24. Despite this, one should keep in mind that over half the predictors predict the test data perfectly. But starting with only the top 24 genes (20 distinct genes) with $n_{top} = 20$ leads to a set of predictors that make an average of 1.45 mistakes, and an average number of genes of 10.95.

The genes found by these methods are mostly a subset of those found previously (Khan et al., 2001). For example with 75 initial genes as described above (fig. 5), the union of all predictor genes found in the top 100 predictors gave a total of 24 genes. These were a subset of the 96 Khan et. al. genes. These are shown in Table 1 (excluding three genes that occur only once among all the predictors). However with the data of fig. 3, we find that out of a total of 25 different genes that comprise all the possible genes used by the 50 predictors, four are different than those found by Khan et. al. Of those four, one of them appear only once, and two of them occur quite frequently in the predictors. One, neurofibromin 2 appears in all predictors, and the other thioredoxin appears in 37 of the 50 predictors. The third, homeobox B7 appears 6 times. Neurofibromin has been associated with tumorogenesis (Reed & Gutmann, 2001). It is believed that thioredoxin may play a role in cancer and Thioredoxin-1 is often associated with aggressive tumor growth (Powis & Montfort, 2001). In a study on multiple carcinogenesis of mouse skin (Chang et al., 1998), Homeobox B7 appears to be expressed at a much lower level than in normal mouse skin. Because this gene only appears in 16% of predictors, this may not be a significant correlation.

**Leukemia Data**

Microarray data was obtained from patients having two types of leukemia, acute lymphoblastic leukemia (ALL), and acute myeloid leukemia (AML). The data here was taken from bone marrow samples and the samples were of different cell types, for example B or T cells and different patient genders. Each sample was analyzed using an Affymetrix microarrays containing expression levels of 7129 genes. The data was divided into 38 training data points and 34 test points.

Using the statistical replication algorithm we evolved the predictors and measured the averaged number of misclassifications made as a function of the number of generations. This is done with an initial pool of 50 genes and the results are shown in fig. 6. The number of mistakes made by the ensemble of predictors plateaus at about 2. The predictors vary in accuracy; there are predictors that make no mistakes and some that make several. There appears to be no way of distinguishing between them short of using the test data. Data with 200 genes, fig. 7, shows a similar pattern but does not completely plateau fluctuating in the average number of mistakes from about 1 to three.

On the other hand using the deterministic evolution algorithm, we find a much faster convergence
to a steady state ensemble of predictors. Using an initial gene pool of 50 and $n_{\text{top}}$ of 100, the number of mistakes goes to about 2 with only three genes in a predictor. This is shown in fig. 8. The lack of convergence to near perfect predictors is in agreement with other work on this data set (Furey et al., 2000; Li & Yang, 2001; Golub et al., 1999).

Varying parameters such as the initial number of genes, $n_{\text{top}}$, and the method of scoring does not lead to a statistically significant improvement in the average number of mistakes made. Also, as the above cases illustrate, the optimum number of genes in a predictor varies between 3 to 25 depending on parameters. This is consistent with recent work on this data where also no clear cutoff in the number of genes needed for an optimal predictor was also found (Li & Yang, 2001).

Discussion

This paper has described a new and highly effective method, GESSES, that reduces the number of genes necessary to perform an accurate classification. We implemented and tested it, producing an ensemble of predictors that use a minimal number of genes to perform a diagnosis of a cancer from microarray data.

There are many different kinds of prediction algorithms that can be used besides the nearest neighbor algorithm that we chose, among them are artificial neural networks, logistic regression, support vector machines which appear to perform similarly.

We have used a nearest neighbor search method for a variety of reasons. It will classify training points perfectly. It makes little in the way of assumptions of how new data extrapolates from old data. And in conjunction with the replication algorithms used here it is quite efficient because it “learns” rapidly. However which kind of predictor that is used is not the most important part of this work and the replication algorithm could be implemented with anyone of the prediction methods mentioned above.

The main point is that evolutionary algorithms can be used to determine minimal gene sets for tissue classification. By starting off with an initial pool of candidate genes, an ensemble of predictors is evolved on training data. Each predictor uses a different set of genes and its fitness is scored by analyzing how well it separates the training data into separate classes. The system evolves converging to a set of predictors that can be evaluated using test data.

In the case of SRBCT data (Khan et al., 2001), this method was able to find predictors using fewer than 15 genes that were able to reliably classify test data into one of four groups. Some of the genes found were different than the 96 found earlier (Khan et al., 2001) to do this classification and may be of biological significant. The optimum number of genes to use in a predictor is approximately $12 \pm 2$.

In the case of leukemia data (Golub et al., 1999), less useful information can be obtained. It is probably not possible to use the training data to reliably construct a perfect predictor. It is clear that more data is needed before the same level of prediction can be achieved as with the SRBCT data. This is in accord with other groups findings (Golub et al., 1999; Furey et al., 2000; Li & Yang, 2001). At this point it is not possible to come up with the optimal number of genes needed to predict this data (Li & Yang, 2001).
The main conclusion that one draws from this is that there are many relevant genes in the diagnosis of cancers. However if the data is not complete or is too noisy, it is not possible to exploit this information to its full capacity.

It is hoped that using such a small set of genes could help lead to practical uses of gene expression levels in cancer diagnosis, as it might turn out to be more practical to build devices containing only 15 oligonucleotides rather than thousands. It also might help to further the understanding of how the genes found relate to the biology of these cancers.

Acknowledgments

The author thanks Francoise Chanut for useful discussions.
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Figure 1: The average number of genes for an ensemble of predictors as a function of the number of generations, for SRBCT data [Khan et al., 2001]. The number of genes used here was 50, and the algorithm used was a statistical replication algorithm ($n_m = 2$).
Figure 2: The average number of mistakes made as a function of the average number of genes in a predictor for the same parameters as in fig. [1]
Figure 3: The average number of genes for an ensemble of predictors as a function of the number of generations for SRBCT data (Khan et al., 2001). The number of genes used here was 50, and the algorithm used was deterministic described in the text.
Figure 4: The average number of mistakes made as a function of the average number of genes in a predictor for the same parameters as in fig. [3].
Figure 5: The average number of mistakes made as a function of the average number of genes in a predictor for an initial pool of 75 genes SRBCT data (Khan et al., 2001). The parameters are described in the text.
Figure 6: The average number of mistakes for an ensemble of predictors as a function of the average number of genes, for the leukemia data (Golub et al., 1999). The number of genes used here was 50, and the algorithm used was a statistical replication algorithm ($n_m = 2$). Note the curve is not singled valued because as the predictor evolves, the average number of genes and number of mistakes can increase due to statistical fluctuations.
Figure 7: The average number of mistakes for an ensemble of predictors as a function of the average number of genes, for the leukemia data \cite{Golub99}. The number of genes used here was 200, and the algorithm used was a statistical replication algorithm ($n_m = 2$).
Figure 8: The average number of mistakes for an ensemble of predictors as a function of the average number of genes, for the leukemia data (Golub et al., 1999). The number of genes used here was 200, and the algorithm used was a deterministic algorithm.
| id#     | gene description                                                                 |
|--------|----------------------------------------------------------------------------------|
| 365826 | growth arrest-specific 1                                                          |
| 298062 | "troponin T2, cardiac"                                                            |
| 383188 | recoverin                                                                         |
| 296448 | insulin-like growth factor 2 (somatomedin A)                                      |
| 769959 | "collagen, type IV, alpha 2"                                                      |
| 377461 | "caveolin 1, caveolae protein, 22kD"                                              |
| 325182 | "cadherin 2, N-cadherin (neuronal)"                                               |
| 1473131| "transducin-like enhancer of split 2, homolog of Drosophila E(sp1)"               |
| 207274 | Human DNA for insulin-like growth factor II (IGF-2); exon 7 and additional ORF    |
| 357031 | "tumor necrosis factor, alpha-induced protein 6"                                   |
| 812105 | transmembrane protein                                                             |
| 241412 | E74-like factor 1 (ets domain transcription factor)                                |
| 183337 | "major histocompatibility complex, class II, DM alpha"                             |
| 796258 | "sarcoglycan, alpha (50kD dystrophin-associated glycoprotein)"                    |
| 866702 | "protein tyrosine phosphatase, non-receptor type 13 (APO-1/CD95 (Fas)-associated phosphatase)" |
| 770394 | "Fc fragment of IgG, receptor, transporter, alpha"                                 |
| 52076  | olfactomedinrelated ER localized protein                                           |
| 609663 | "protein kinase, cAMP-dependent, regulatory, type II, beta"                       |
| 814260 | follicular lymphoma variant translocation 1                                        |
| 784224 | fibroblast growth factor receptor 4                                               |
| 295985 | ESTs                                                                              |

Table 1: Genes found that perfectly predict SRBCT samples