Kohonen neural networks and genetic classification

Daniela Bianchi * Raffaele Calogero† Brunello Tirozzi‡

Abstract

We discuss the property of a.e. and in mean convergence of the Kohonen algorithm considered as a stochastic process. The various conditions ensuring the a.e. convergence are described and the connection with the rate decay of the learning parameter is analyzed. The rate of convergence is discussed for different choices of learning parameters. We proof rigorously that the rate of decay of the learning parameter which is most used in the applications is a sufficient condition for a.e. convergence and we check it numerically. The aim of the paper is also to clarify the state of the art on the convergence property of the algorithm in view of the growing number of applications of the Kohonen neural networks. We apply our theorem and considerations to the case of genetic classification which is a rapidly developing field.

1 Introduction

Data clustering ([1]-[5]) is a basic technique in gene expression data analysis since the detection of groups of genes that manifest similar expression patterns might give relevant information. Therefore it is important to have a good control on the properties of clustering algorithms. The Kohonen algorithm ( or Kohonen neural network) ([6]-[8]) is currently used in this field. The Kohonen neural networks are different from the other neural networks like back propagation or the Hopfield model ([9]-[12]). The main difference is that there is only a single layer of units (named neurons) and the output of the network is just a vector or a scalar associated with each neuron called weight vector. These networks are commonly used for classifying sets of experimental data. The weight vector associated with the neuron represents a characteristic vector of a certain subset of the data. The set of these subsets constitutes a disjoint partition of the measures. The sets of the partition are also called clusters and in the applied science there are many different algorithms which construct clusters from a data set. Many of these algorithms have the drawback that they depend on arbitrary choice of some parameters and therefore the clustering results might be non unique. The main feature of clustering by means of the Kohonen algorithm is that it depends only on the choice of a special function, the learning parameter, which has been extensively characterized. The process of individuation of the weights is called the learning process and the Kohonen algorithm is a special learning process. This algorithm consists in extracting at each time step $n$ a number or a vector from the data set and subsequently the nearest weight to this data is modified of a quantity proportional to the difference among these two vectors multiplied by a parameter. This parameter is the learning parameter, and it must decrease with $n$. The convergence of the learning process strongly depends on the rate of decay of the learning parameter and the investigation of this point is one of the main topics of this paper. An important characteristic of the Kohonen algorithm is the Self Organization(SO) which can be understood as the fact that the sequence of the weights converges to a unique limit independently from the chosen sequence of the data presented to the network and from the initial values of the weights. In the language of the stochastic processes we can express this fact by observing that the sequence of the weights is a stochastic process and SO is equivalent to the a.e. convergence of the learning process. This property is rather strong and it is supposed to hold in many applications of the Kohonen networks but unfortunately it is not trivial at all. This is especially true for genetic

*Department of Physics, University "La Sapienza", Rome; E-mail: danielabianchi12@gmail.com
†Bioinformatics and Genomic Unit, University of Turin, Turin; E-mail: raffaele.calogero@unito.it
‡Department of Physics, University "La Sapienza", Rome; E-mail: brunello.tirozzi@roma1.infn.it
application where the set of clusters (atoms) describes different cell conditions or different genes function. In order to have a real biological meaning the classification should be independent on the initial conditions of the weights and from the input sequence. So it is worth investigating, both theoretically and numerically, the connection among the a.e. convergence and the possible choices of the learning parameter \( \eta(n) \) and the different versions of the Kohonen algorithm. There are already many important results on this subject ([13]-[28]). All these results show that there is a critical dependence of the a.e. convergence on the probability distribution of the data, on the choice of the learning algorithm and on the velocity to approach zero by \( \eta(n) \). In this paper we generalize the results obtained in the paper of Feng and Tirozzi ([25]) relaxing the condition on the convergence of the series \( \sum_n \eta(n)^2 \) (but of course it is assumed that \( \eta(n) \rightarrow 0 \)), so only the condition \( \sum_n \eta(n) \rightarrow \infty \) remains. The condition \( \sum_n \eta(n)^2 < \infty \) is used in all the other versions of the theorems of convergence, but we have verified numerically that it implies a too rapid convergence to zero of the learning parameter. So the good decrease rate for \( \eta(n) \) is to go to zero more slowly than \( 1/n \). But our theorem does not exclude the \( 1/n \) decay rate since it also satisfies the condition \( \sum_n \eta(n) \rightarrow \infty \). Thus this theorem gives a support to the property of a.e. convergence for the right decay of \( \eta \) but it is uncompleted because we cannot show that the stronger condition \( \sum_n \eta(n)^2 < \infty \) spoils the a.e. convergence. The previous results also are troublesome because we are faced with the fact that a theorem with a defined proof of convergence does not correspond to the numerical simulations. The only thing we can say is that at least our version of the convergence theorem picks the right decrease property. There is a well known general explanation about the right choice of the rapidity of the learning parameter decay which is connected with the existence of meta-stable points. In analogy with the Simulated Annealing (SA) we can say that the learning parameter corresponds to the temperature and it is a well known fact that a too rapid decrease of the temperature in the SA makes the algorithm stop on the local minima of the energy function. The unlucky situation is that in the case of the Kohonen algorithm there is no such a function. In many proofs of the convergence one can find some functional with a similar property but they are not the energy or the Liapunov function. The other important question tackled in this paper is about the rate of the convergence of the algorithm: since the condition \( \sum_n \eta(n) \rightarrow \infty \) can be satisfied by many different \( \eta(n) \) we compare the different choices analyzing the velocity of approach to the limit of the corresponding algorithm. This question is important in any case but has special relevance in gene clustering where the data set is the set of expression levels of \( M \) genes, \( M \) being rather large than to the application of the microarrays technique. The meaning of \( M \) in our construction is the maximum number of iterations of the learning process. Another question considered in this paper is the analysis of the relation of the a.e. convergence with the probability distribution of the data and also with the different versions of the Kohonen algorithm. We then apply all these results to the problem of clustering and classifying the great number of genes revealed in the microarrays experiments. The possibility of applying clustering algorithms (not only the Kohonen algorithm) in genetics appeared with the development of the DNA microarrays technology. The micro-array allows to monitor simultaneously the expression levels of thousands of genes during important biological processes. Elucidating the patterns hidden in the gene expression data is a tremendous opportunity for functional genomic. However, because of the large number of genes and complexity of biological networks, it is difficult to interpret the resulting mass of data; so the clustering techniques become essential in data mining process for identifying interesting distributions and patterns in the underlying data.

Clustering algorithms have simplified the grouping of genes with similar biological expression. Co-expressed genes found in the same cluster suggest functional similarities. Gene clustering also becomes the first step to uncover the regulatory elements in transcriptional regulatory networks. Co-expressed genes in the same cluster might be involved in the related cellular process and strong expression pattern correlation between those genes suggests co-regulation.

There is a large literature on cluster analysis and genetic one ([11]-[5]): numerous approaches were proposed on the basis of different quality criteria and not all the algorithms are well founded. In addition the results of the algorithms depend strongly on many arbitrary choices, for example on the initial conditions and the value of the threshold.

The main topic of the last section of this paper is an application of the Kohonen algorithm to a concrete problem of gene classification. The aim is to find the genes which are over expressed during the treatment of tumor cells of mice using a clustering technique that has the minimum
arbitrary choices.
The analysis made in the first sections of this paper convinced us to use the Kohonen algorithm.
We compare the results obtained with the Kohonen algorithm to this problem with the ones obtained using the PCA (Principal component analysis) and Hierarchical clustering algorithm (30). This is the first step of a larger work of comparing the results of gene classification obtained by means of different algorithms. We think that this work is necessary in order to validate the gene clustering.

Another important issue is the variability of the expression levels of genes obtained by different samples which cannot be considered equal. For economic and time reasons it is difficult to have more than three biological realizations of the experiment and this is the origin of an error in the data. The errors influence the structure of the clusters so it is possible that a gene changes cluster if we take into account this error in the analysis. In our work we have included explicitly this effect and evaluated its influence on the results.

The structure of the paper is the following. In Section 2, after a short intuitive introduction, we show the algorithm and explain its properties using a precise mathematical formulation, enunciate the theorems and give the proofs. In Section 3 we show the results of the numerical simulations. In Section 4 we show the applications to the mice data and our results. In Section 5 we give our conclusions.

2 The Kohonen Network

2.1 An intuitive description

The Kohonen Network ([6]-[8]) is formed by a single layered neural network. The data are presented to the input and the output neurons are organized with a simple neighborhood structure. Each neuron is associated with a reference vector (the weight vector), and each data point is "mapped" to the neuron with the "closest" (in the sense of the Euclidean distance) reference vector. In the process of running the algorithm, each data point acts as a training sample which directs the movement of the reference vectors towards the value of the data of this sample. The vectors associated with neurons, called weights, change during the learning process and tend to the characteristic values of the distribution of the input data. The characteristic value of one cluster can be intuitively understood as the typical value of the data in the cluster and will be defined more precisely in the next subsections. At the end of the process the set of input data is partitioned in disjoint sets (the clusters) and the weight associated with each neuron is the characteristic value of the cluster associated with the neuron in one dimensional case, which is the case of interest to us. We limit our analysis to this case because the condition of convergence of the algorithm is easier to check, the cluster of the partitions are easier to visualize and it is not difficult to compare the behavior of the genes in the clusters corresponding to the different biological conditions. Each neuron individuates one cluster, the physical or biological entities with measure values belonging to the same cluster are considered to be involved in the same cellular process. Thus the genes with expressions belonging to the same cluster might be functionally related.

The following points show the main properties which make the Kohonen network useful for clustering:

1. Low dimension of the network and its simple structure.
2. Simple representation of clusters by means of vectors associated with each neuron.
3. Topology of the input data set is somehow mapped in the topology of the weights of the network.
4. Learning is unsupervised.
5. Self-organized property

The points 1)-2) are simple to understood and many examples are shown in the Section 3. The point 3) means that neighboring neurons have weight vectors not very different from each other. The point 4) means that there is no need to have an external constraint to drive the weights towards their right values beside the input to the network and that the learning process finds by
itself the right topology and the right values. This holds only if the learning process with which the network is constructed converges a.e. or if the mean values are taken. The self-organization is formulated in the current literature referring to some universality of the structure of the network for a given data set. It is connected to the point 3) and is also a consequence of a.e. convergence or of the convergence of the average of the weights over many different learning processes.

2.2 Exact definition

In this subsection we give the definitions using exact mathematical terms. We restrict ourselves to the particularly simple one dimensional case which is the most interesting for our applications.

First we show how the Kohonen network is used for classification and then what is the process of its construction. Let \( I = I_1, \ldots, I_N \) be a partition of the interval \((0, A)\) of the possible values of the expression levels in the intervals \( I_i, \bigcup I_i = (0, A) \) and \( I_i \cap I_j = \emptyset \).

Suppose that the construction of the Kohonen network has been already done and the weights or the characteristic values of the clusters which will be exactly defined below. Then a data \( \xi \) is said to have the property \( i \) if \( \xi \in I_i \).

The classification error is

\[
|\xi - \omega_i|
\]

Then the global classification error \( E \) of the network is

\[
E = \frac{1}{T} \sum_{i=1}^{N} \int_{I_i} \|\xi - \omega_i\|^2 f(\xi) \, d\xi
\]

(2.2.1)

where \( f(\xi) \) is the density of probability distribution of the input data and \( T = \sum_{i=1}^{N} |I_i| \), with \( |I_i| \) is the number of data in the set \( I_i \).

The partition \( I = I_1, \ldots, I_N \) is optimal if the associated classification error \( E \) is minimal. The characteristic vectors \( \omega_i \) are the values which minimize \( E \). Before giving exact definitions let us explain in simple terms the procedure for determining the sets \( I_i \) and the associated weights \( \omega_i \).

Let \( x(1), \ldots, x(P) \) be a sequence of values randomly extracted from the data set, distributed with the density \( f(x) \) and take randomly the initial values \( \omega_1(0), \ldots, \omega_N(0) \) of the weights. When an input pattern \( x(n), n = 1, \ldots, P, \) is presented to the network all the differences \( |x(n) - \omega_i(n-1)| \) are computed and the winner neuron is the neuron \( j \) with minimal difference \( |\xi(n) - \omega_j(n-1)| \).

The weight of this neuron is changed in a way defined below, or, in some cases, the weights of the neighboring neurons are changed. Then this procedure is repeated with another input pattern \( x(n+1) \) and with the new weights \( \omega_i(n) \) until the weights \( \omega_i(n) \) converge to some fixed values for \( P \) large enough.

In this way we get a random sequence \( \omega(n) = (\omega_1(n), \ldots, \omega_N(n)) \) which converges a.e, under suitable conditions on the data set, with respect to the choice of the random sequence of data and the random choice of the initial conditions of the weights, \( n \) is the number of iterations of the procedure. The learning process is the sequence \( \omega(n) \) and the S.O. (self-organizing property) coincides in practice with the almost everywhere convergence of \( \omega(n) \). The learning process converges somehow to the optimal partition in the Kohonen algorithm. In fact the algorithm can, with some approximation, be viewed as a gradient method applied to the function \( E \):

\[
\omega_i(n+1) = \omega_i(n) + \eta(n)[\xi(n) - \omega_i(n)]
\]

\[
\sim \omega_i(n) - \frac{1}{2} \eta(n) \nabla_{\omega_i(n)} E
\]

In one dimension the Kohonen algorithm in the simplest version of the winner-take-all case is:

1. Fix \( N \).
2. Choose randomly at the initial step \( n = 0 \) the \( \omega_i \) \( (0 \leq i \leq N) \).
3. Extract randomly the data \( \xi(1) \) from the data set.
4. Compute the modules
\[ |\omega_i(0) - \xi(1)| \quad i = 1, \ldots, N \]

5. Choose the neuron \( v \) such that
\[ |\omega_v(0) - \xi(1)| \]

is the minimum distance. \( v \) is the winner neuron

6. Update only the weight of the winner neuron:
\[ \omega_v(1) = \omega_v(0) + \eta(1)(\xi(1) - \omega_v(0)) \]

7. \( n = n + 1 \)

One of the basic property of the Kohonen network is that the weights are ordered if the learning process converges.

We remind the definition of the order of a one dimensional configuration:
\[ |r - s| < |r - q| \iff |\omega_r - \omega_s| < |\omega_r - \omega_q|, \quad \forall r, s, q \in \{1, 2, \ldots, N\} \]

the order holds also for the other inequality \( |\omega_r - \omega_s| > |\omega_r - \omega_q| \). Then:

The ordering property is:

If the Kohonen learning algorithm applied to one dimensional configuration of weights converges the configuration order itself at a certain step of the process. The same order is preserved at each subsequent step of the algorithm.

This property allows to check when the algorithm converges since the final configuration of weights must be also ordered and it is a necessary property for a.e. convergence. We also check the remarkable property proved by Kohonen ([6]-[8]) that the mean process \( \omega(n) \), i.e. the process obtained by averaging with respect different choices of the sequence \( x(1), \ldots x(P) \) is always converging. But for getting the a.e. convergence from the convergence of the mean values additional hypothesis must be used and the discussion and the applications of these results to a case of genetic classification is the main topic of this paper.

2.3 General formulation

We describe now the Kohonen algorithm in more general terms for allowing the treatment of all the possible cases.

The Kohonen network is composed by a single layer of output units \( O_i, i = 1, \ldots, N \) each being fully connected to a set of inputs \( \xi_j(n), j = 1, \ldots, M \). An \( M \) dimensional weight vector \( \omega_i(n) = (\omega_{ij}(n), j = 1, \ldots, M) \) is associated with each neuron. \( n \) indicates the \( n \)-th step of the algorithm.

We assume that the inputs \( \xi_j(n), j = 1, \ldots, M \) are independently chosen according to a probability distribution \( f(x) \). For each input \( \xi_j(n), j = 1, \ldots, M \) we choose one of the output units, called the winner. The winner is the output unit with the smallest distance between its weight vector \( \omega_v(n) \) and the input

\[ ||\omega_v(n) - \xi(n)|| \]

where \( ||.|| \) represents Euclidean norm. Let \( 1(\ldots) \) be the function
\[ 1(\omega_v(n), \xi(n + 1)) = 1(||\omega_v(n) - \xi(n + 1)|| < ||\omega_v(n) - \xi(n)||, j \neq v) \]

where \( 1_A \) is the characteristic function of the event \( A \), i.e, \( 1_A(x) = 1 \) if \( x \in A \) and \( 1_A(x) = 0 \) if \( x \notin A \).

This function selects the event in which the weight of the neuron \( v \) is the nearest to the input data \( \xi(n) \) and it is necessary for writing the learning process in a compact form. The generalized Kohonen algorithm updates the weights of the neurons belonging to a given neighbor of the winner neuron:

\[ \omega_{ij}(i + 1) = \omega_{ij}(n) + \eta(n)1(i, v)1(\omega_v(n, \xi(n + 1)) (\xi_j(n + 1) - \omega_{ij}(n)) \quad (2.3.1) \]
\[ \omega_i(n+1) = \omega_i(n) + \eta(n) \Gamma(i, v) \left[ \omega_v(n), \xi(n) \right] \left( \xi(n+1) - \omega_i(n) \right) \]  \hspace{1cm} (2.3.2)

where \( \eta(n) \) is the positive learning parameter \( \eta(0) < 1, \eta(n) \geq \eta(n+1) \) and \( \Gamma(i, v) \) is a non increasing function of \( |i - v| \), the distance among the neuron \( i \) and \( v \) on the lattice where the neurons of the network are located.

This version is more general than the winner-take-all rule explained before. Not only the weight of the winner neuron is updated but also the weights of the neurons which belong to a neighborhood defined by the function \( \Gamma(i, v) \). We discuss various choices of the function \( \Gamma(i, v) \) below. After the learning procedure is finished, the set of input vector will be partitioned into non overlapping clusters. This means that a new signal \( \xi(n+1) \) is classified as the pattern \( i \) if and only if

\[ ||\omega_i - \xi(n+1)|| \leq ||\omega_j - \xi(n+1)||, \ j \neq i \]

Let us introduce the definition of Voronoi tessellation \( \Pi(y) = (\Pi(y), i = 1, \ldots, N) \) associated with a family vectors \( y_1, \ldots, y_N \in \Omega \), \( \Omega \) being a given compact of \( \mathbb{R}^M \).

**Definition 2.1.** For a given compact subset \( \Omega \subseteq \mathbb{R}^M \), the Voronoi tessellation \( \Pi(y) = (\Pi(y), i = 1, \ldots, N) \) associated with a family of vectors \( y_1, \ldots, y_N \) is the partition of \( \Omega \):

\[ \Pi(y)_i = \{x, \|y_i - x\| \leq \|y_j - x\|, j \neq i\} \quad i = 1, \ldots, N \]  \hspace{1cm} (2.3.3)

Therefore a Voronoi cell of an unit \( i \) contains those vectors which are closer to the weight \( \omega_i \) than to the other weights. The characteristic values mentioned before are the limit of the sequences of the vectors \( \omega_i(n) \) defined by the above algorithm and are weights of the Voronoi tessellation obtained in the limit.

A crucial point of the algorithm is the choice of the neighborhood function \( \Gamma(i, v) \) of the winner neuron. It determines the region around the winner neuron where there are the neurons which update their weight vectors together with the winner neuron. A convenient choice is the finite region of activation of the winner neuron, i.e. \( \Gamma = \Lambda \) where:

\[ \Lambda(i, v) = \{ \begin{array}{ll} 1 & \text{if } |i - v| \leq s \\
0 & \text{otherwise} \end{array} \]  

where \(|.|\) represents the distance between the neuron \( i \) and the winner neuron \( v \).

If \( s = 1 \) and the neural network is one dimensional, the region of activation includes the winner and the two nearest units (figure 1); if the network is designed in two dimension then the range includes the eight nearest neighbor units near the winner.

If \( \Lambda(i, v) = \delta_{iv} \), the algorithm coincides with the winner takes all algorithm we described in the previous section.

![Figure 1: Neighborhood function \( \Lambda(i, v) \)](image-url)
function $h$ defining a region around the winner neuron with amplitude decreasing with the number of iterations of the learning process:

$$h(i, v, n) = \exp\left(-\frac{|i - v|^2}{\sigma(n)^2}\right)$$

(2.3.4)

where $\sigma(n)$ is a decreasing function. A commonly used choice is:

$$\sigma(n) = \sigma_i \left(\frac{\sigma_f}{\sigma_i}\right)^{\frac{n}{n_{max}}}$$

where $n_{max}$ is maximum number of iterations of the algorithm and $\sigma_f, \sigma_i$ are respectively the final and initial value of the parameter $\sigma$ (figure 2).

![Figure 2: Neighborhood function $h(i, v, n)$](image)

### 2.3.1 The theorem of convergence

The first result about the algorithm convergence was found by Kohonen ([7]). He concentrated on one-dimensional mapping and demonstrated that the weights converge in mean to the limit values. Although the result is enunciated as a.e. convergence in this paper only the convergence in mean is proven. The convergence in mean is obtained by making the average of the weights on many different sequences of patterns $x(n)$. The ordering of the weights has been proved in ([7]) for the winner-take-all process.

In the paper of Erwin et al. ([16],[17]) there is a proof of ordering for one-dimensional case which holds for any neighborhood function which is monotonically decreasing with distance and in the case of non uniformly distributed input.

Many other authors ([13],[19],[21],[22],[23],[25],[28]) investigated the convergence properties of the Kohonen algorithm in one and more dimensions, someone by viewing the weight values as states of a Markov process, others using the ordinary differential equations for the mean values of the network. But the main results have been limited to one dimensional map where the property of order is valid and under certain conditions on $\eta(n)$, the expectation of the values weights converges to a unique value. The existence and uniqueness of the minimum is ensured by the existence of a unique minimum of some functional, but the existence of the minimum is difficult to check for non uniform distribution of the input values especially in the multidimensional case.

In more than one dimension, despite the robustness of the algorithm which has been used successfully in many different application area, there is still no proof of a necessary and sufficient condition for the convergence of the algorithm. There are proofs of sufficient conditions and only a few for the multi dimensional case, see for example Feng and Tirozzi ([25]), Lin and Si ([19]), Sadeghi ([23]). Lin and Si have shown that the distribution of the weight values converge to a stationary state introducing and studying the same objective function proposed by Ritter and Schulten [21]. In the paper of Feng and Tirozzi the convergence problem of the Kohonen feature mapping algorithm has been proven by using stochastic approximation theory. But in all these
papers the rate of decrease of the learning parameter is too fast and so these theorems are contradicted by numerical results. Only in the paper of Feng and Tirozzi it is mentioned explicitly that the rate of decrease of the learning parameter of these theorems is too fast and there is a proposal for a slower decay. In this paper we proof that there is a.e. convergence if the rate is the one of numerical simulations, but we can show only the sufficiency of this condition. Moreover a condition of the existence of a global attractive minimum is always required.

If there is no global minimum there is no a.e. convergence and the algorithm remains stacked, as in the case of simulated annealing, in some points which might not even be ordered and then the convergence is obtained only by averaging with respect to the sequences of learning examples, which is happening for the genetic data in general. Now we start to expose the definitions and concepts used in our proof. We first explain the definitions used in the book of Nevel’son and Has’minski (20) which will be used in the proof of our main theorem. Let \( \xi(k), \ k \leq n \) be the sequence of random patterns presented to the network during the learning and \( \mathcal{F}_n \) the \( \sigma \)-algebra generated by them, \( \mathbb{E}(\xi|\mathcal{F}_n) \) is the conditional expectation of the random variable \( \xi \) with respect to the sigma algebra \( \mathcal{F}_n \).

Our aim is to prove that the process of the weights \( \omega(n) \) converges to a certain set \( B \subseteq \mathbb{R}^{N \times M} \) (the limit set), so we need the definitions summarized in the following list:

**Definition 2.2.**

1. A distance between vectors \( y \in \mathbb{R}^M \) and \( \omega_i \in \mathbb{R}^M \), \( \rho(\omega_i, y) \), with \( i = 1, \ldots, N \).
2. A distance from the point \( \omega(n) \) and the set \( B: \rho(\omega(n), B) = \inf_{y \in B} \rho(\omega, y) \).
3. An \( \varepsilon \) neighborhood of \( B \), \( U_\varepsilon(B) = \{ \omega: \rho(\omega, B) < \varepsilon \} \).
4. The complementary set of this neighborhood \( V_\varepsilon(B) = \mathbb{R}^{N \times M} \setminus U_\varepsilon(B) \).
5. The intersection of the complementary set with a sphere of radius \( R \): \( V_{\varepsilon,R}(B) = V_\varepsilon(B) \cap \{ \omega(n) : \omega(n) R \} \).
6. A positive definite Lyapunov function \( W(n, \omega) \), \( \omega \in \mathbb{R}^{N \times M} \).
7. An operator \( LW(n, \omega) = \mathbb{E}(W(n+1, \omega(n+1)) - W(n, \omega(n))|\mathcal{F}_n) \) defining a kind of first difference of the Lyapunov function by means of conditional expectation.
8. A negative function \( g(n, \omega) \) used for bounding the increments of the Lyapunov function \( W(n, \omega) \) such that

\[
\inf_{n \geq Q, \omega \in V_{\varepsilon,R}(B)} [-g(n, \omega)] > 0
\]

for all \( R > \varepsilon > 0 \) and some \( Q = Q(\varepsilon, R) \).

Let us briefly comment these definitions.

1) As we have seen before \( \omega \) and \( y \) are \( \mathbb{R}^M \) vectors and since we have to compare their difference it is necessary to introduce the module of these vectors.
2) In the general case the limit point might be a set so the distance of a point from a set must be defined.
3) As is usual in the theory of limits one needs to find a neighborhood \( U_\varepsilon(B) \) of the limit points \( B \) which differ from \( B \) by a small portion.
4) It is also necessary to introduce the complementary set \( V_\varepsilon(B) \) of this neighborhood.
5) For doing the estimates of asymptotic limits of series or functions it is useful to introduce a spherical subset \( V(B)_{\varepsilon,R} \) of \( V_\varepsilon(B) \).
6) In analogy with the theory of stability in order to show the convergence of a trajectory of a dynamical system it is useful to have a Liapunov function and compute its increments. In this case we do not have an usual dynamical system but a stochastic sequence.
7) The consequence of this fact is that the derivative (or increments) of the Liapunov function is not the usual one but is a conditional expectation. The convergence holds for the sequence \( W(n, \omega) \) as a consequence of Doob’s theorem of convergence for martingales but it is difficult to use the concepts of local and global minimum in this situation. In our theorem the concept of global minimum in the classical sense is introduced but for the bounding function \( g(n, \omega) \).

We will use this theorem of (20) in our proof of the a.e. convergence:
Theorem 2.1. Suppose that there exist a function $W(n, \omega) \geq 0$ such that:

$$LW(n, \omega) \leq \eta(n)g(n, \omega)$$  \hspace{1cm} (2.3.6)

where $n \geq 0$, $\omega \in \mathbb{R}^{N \times M}$ and $g$ the function which satisfies the above statement  \hspace{1cm} (2.3.5)

Moreover let :

$$\sum_{n=1}^{+\infty} \eta(n) = +\infty$$ \hspace{1cm} (2.3.7)

and:

$$\inf_{n \geq 0} W(n, \omega) \to +\infty$$ \hspace{1cm} (2.3.8)

Then, considering the previous definitions:

$$P\{\sup_{n} |\omega(n)| = R < +\infty\} = 1$$ \hspace{1cm} (2.3.9)

$$P\{\sum_{u=0}^{+\infty} \eta(u)[-g(u, \omega(u))] < +\infty\} = 1$$ \hspace{1cm} (2.3.10)

$$P\{\liminf_{n \to +\infty} \rho(\omega(n), B) = 0\} = 1$$ \hspace{1cm} (2.3.11)

We can say that a random process $\omega(n)$ converges a.e. to a limit set $B$ if it is possible to find a Liapunov function $W(n, \omega(n))$ of the process such that the conditional expectation of its increments are less than a function $g(n, \omega)$ multiplying the learning parameter $\eta(n)$, then $\omega(n)$ converges to $B$, if the function $g$ is negative in a certain spherical neighborhood of $B$ and if the learning parameter decreases not so quickly. So it is enough that

$$\lim_{n \to +\infty} \eta(n) = 0$$

in order that the a.e. convergence of the weights holds. The interesting fact is that the stronger condition

$$\sum_{n=1}^{+\infty} \eta(n)^2 < +\infty.$$ is not introduced. The result of this theorem is neat because the condition

$$\lim_{n \to +\infty} \eta(n) = 0$$

is the one used in the numerical applications. In Section 3 we will give many examples of "good" and "bad" decay of $\eta(n)$. The choice of $\eta(n)$ is important also for the speed of convergence of the process. Another key role for the a.e. convergence is the form of the probability distribution of the data as it will be clear from the theorem we present below.

In order to understand it we need other definitions. Let us introduce a function $g$ which is the leading term of the super martingale difference given in the proof of theorem 2.2. It is a particular realization of the function $g$ used in the theorem of Nevel’son and Has’minskii:

$$g(y_1, y_2, ..., y_N; \omega_1, \omega_2, ..., \omega_N) = \sum_{i=1}^{N} (y_i - \omega_i) \cdot \sum_{k} \left( \int_{\Pi(y)_k} \Lambda(k, i) (x - y_i) f(x) dx \right).$$ \hspace{1cm} (2.3.12)

where $\omega_i(n) = (\omega_{ij}(n), j = 1, ..., M, i = 1, ..., N)$ and $y_i(n) = (y_{ij}(n), j = 1, ..., M, i = 1, ..., N) \in \mathbb{R}^{M \times N}$ $f$ is the density of the probability distribution of the data with support on a compact set $\Omega$ of $\mathbb{R}^M$. $\Pi(y)$ is the Voronoi tessellation associated with $y$ (see (2.3.3)). $(y_i - \omega_i) \cdot (x - y_i)$ is the $M$-dimensional scalar product.

We define also:

$$\Theta \equiv \{\text{the set of all Voronoi tessellations associated with } \{\omega_1(n), ..., \omega_N(n)\} \text{ for all } n\}$$

For $y \in \mathbb{R}^M$ we use the convention that $y \in \Theta$ implies that there exists a Voronoi tessellation $\Pi(y)$ such that $\{\Pi(y)_i, i = 1, ..., N\} \in \Theta$. Finally we can enunciate our theorem:
Theorem 2.2. Let the vectors \( \omega(n) \in \mathbb{R}^{M \times N} \) be updated by the Kohonen algorithm \[2.3.2\]

\[ \omega_i(n+1) = \omega_i(n) + \eta(n) \Delta(i, v) \tilde{I}(\omega_i(n), \xi(n+1)) \cdot (\xi(n+1) - \omega_i(n)) \]

if there exists a unique point \( \tilde{\omega} = (\tilde{\omega}_1, ..., \tilde{\omega}_N) \in \mathbb{R}^{M \times N} \) such that for each \( y = (y_1, y_2, ..., y_N) \):

\[ g(y_1, y_2, ..., y_N; \tilde{\omega}_1, ..., \tilde{\omega}_N) \leq 0 \quad \forall y \in \Theta \] \[ (2.3.13) \]

where the equality holds if and only if \( y_i = \tilde{\omega}_i \quad i = 1, ..., N \) and:

\[ \sum_{n=1}^{+\infty} \eta(n) = +\infty \quad \lim_{n \to +\infty} \eta(n) = 0 \] \[ (2.3.14) \]

then we almost everywhere have:

\[ \lim_{n \to +\infty} \omega_i(n) = \tilde{\omega}_i \quad i = 1, ..., N \]

Remark 1. This theorem is interesting because the rate of decay of \( \eta(n) \) is the one used in simulations but it is still not enough because the full proposition should exclude the decays which are not used in the simulations i.e. the ones such that

\[ \sum_{n=1}^{+\infty} \eta(n)^2 < +\infty. \]

This last condition is often required in the proofs of theorem about the convergence of Kohonen algorithm, but we have checked in our simulation that there is no convergence. For example if we use \( \eta(n) = \frac{1}{n} \) the limit values of weights are not ordered at the end of the learning process for any initial condition (that is for any random choice of weights at the beginning of the algorithm). This result contradicts that one of Sadeghi \([23]\). In his paper he made a numerical check but it is not enough since he has proven directly only the convergence in mean and not the a.e. convergence and in addition in his simulation he started from ordered weights.

Remark 2. Although the theorem is formulated in the multi-dimensional case we use it in one dimension because the condition \[2.3.13\] is not easy to check in the general case. For \( M = 1 \) it has been seen in the paper \([25]\) that, if the distribution of the data is uniform and the data belong to the interval \((0, 1)\), the clusters are intervals of amplitude 0.1 for \( N = 10 \). They are centered around the points \((0.5, 1.5, ..., 1)\). If the data are gaussian distributed, as in the biological case, there is no unique point satisfying condition \[2.3.13\] and other arguments must be used. We show in Section 3 that, choosing \( \eta(n) \) in a particular way, it is still possible to have a.e. convergence but there is no theorem justifying this result.

Proof

The proof goes like in the paper \([25]\). Let \( B \) be the point \( \tilde{\omega} \) of the theorem, \( U_\varepsilon(B) \) be the \( \varepsilon \) spherical neighborhood of \( \tilde{\omega} \), \( \tau(\varepsilon) \) the first \( n \) for which the process \( \omega(n) \) enters in \( U_\varepsilon(B) \). Let \( \sigma_n \) be the stopping time

\[ \sigma_n \equiv \tau(\varepsilon) \land n = \min(n, \tau(\varepsilon)). \]

The function \( W(n, \sigma_n) \) of the theorem of Nevel’son and Has’minskii for the case of the Kohonen algorithm is

\[ W(n, \omega(n)) = \sum_{i=1}^{N} \| \omega_i(\sigma_n) - \tilde{\omega}_i \|^2 \]

In effect the condition \[2.3.6\] on the function \( W(n, \omega(\sigma_n)) \) is nothing other than the non negative super martingale condition, so if it is possible to show this condition it is possible to apply the convergence property of martingales.

So we start proving:

\[ \sum_{i=1}^{N} \mathbb{E}[\| \omega_i(n+1) - \tilde{\omega}_i \|^2 | \mathcal{F}_n] - \| \omega_i(n) - \tilde{\omega}_i \|^2 \leq 0 \] \[ (2.3.15) \]
The details of the proof can be found in \cite{25} here we give the main results

\[
L W(n, \omega(n)) = \mathbb{E}(W(n+1, \omega(n+1)) - W(n, \omega(n)) | \mathcal{F}_n) = \\
= \sum_{i=1}^{N} \mathbb{E}(\|\omega_{i}(\sigma_{n+1}) - \tilde{w}_{i}\|^2 | \mathcal{F}_n) - \|\omega_{i}(\sigma_n) - \tilde{w}_{i}\|^2 = \\
= \sum_{i=1}^{N} \eta(n)(\omega_{i}(\sigma_n) - \tilde{w}_{i}) \cdot \sum_{v} \int_{\Pi(\omega(\sigma_n))} A(v, i)(x - \omega_{i}(\sigma_n)) f(x) dx + \eta^2(n)g(\omega(\sigma_n)) \\
(2.3.16)
\]

Where:

\[g_1(\omega(\sigma_n)) = \sum_{i=1}^{N} \sum_{v} \int_{\Pi(\omega(\sigma_n))} A(v, i)\|x - \omega_{i}(\sigma_n)\|^2 f(x) dx\]

with \(\omega(n) = (\omega_1(n), \omega_2(n), ..., \omega_N(n))\)

But

\[g_1(\omega(\sigma_n)) \leq \sum_{i=1}^{N} \sum_{v} \int_{\Pi(\omega(\sigma_n))} |A(v, i)|\|x - \omega_{i}(\sigma_n)\|^2 f(x) dx \]

\[\leq \sum_{i=1}^{N} \sum_{v} \int_{\Pi(\omega(\sigma_n))} A f(x) dx \]

\[= N \cdot a \cdot A \equiv \tilde{A} \]

(2.3.17)

since \(|A(v, i)| \leq a, a \geq 0\), and where \(A\) is a positive constant such that:

\[\max\{\|x - \omega_{i}(\sigma_n)\|^2\} \leq A\]

so for (2.3.17) and the conditions (2.3.13) and (2.3.14) we obtain:

\[\lim_{n \to +\infty} \frac{\eta^2(n) g_1(\omega(\sigma_n))}{\eta(n) g(\omega(\sigma_n)))} = 0 \]

(2.3.18)

Hence, for \(n\) large enough, the sign of the term \(2.3.16\) is determined by the sign of \(g(\omega(\sigma_n))\) and so we have:

\[\sum_{i=1}^{N} [\mathbb{E}(\|\omega_{i}(\sigma_{n+1}) - \tilde{w}_{i}\|^2 | \mathcal{F}_n) - \|\omega_{i}(\sigma_n) - \tilde{w}_{i}\|^2] \leq 0\]

From this inequality it follows that

\[W(n, \omega(\sigma_n)) \equiv \sum_{i=1}^{N} \|\omega_{i}(\sigma_n) - \tilde{w}_{i}\|^2\]

is a non negative super-martingale.

Since \(W(n, \omega(\sigma_n))\) is a non negative super-martingale, from the theorem about martingale the limit exists almost everywhere, in addition, by the definition of the stopping time \(\sigma_n\) and assuming that \(\tau(\varepsilon) < C(\varepsilon)\) we have that

\[\exists C > 0 \text{ such that } \lim_{n \to +\infty} W(n, \omega(\sigma_n)) = C \text{ a.e.}\]

Hence we found the main inequality of the theorem of Nevel’son and Has’minskii:

\[L W(n, \omega(n)) \leq \eta(n)g(\omega(n)) \]

(2.3.19)

From (2.3.13) we get that (2.3.5) holds

\[\inf_{\omega(n) \in \bar{V}_n(B)} [-g(\omega(n))] > 0. \]

(2.3.20)
In addition
\[ \inf_{n \geq 0} W(n, \omega(n)) \to +\infty \quad \text{per} |\omega(n)| \to +\infty \quad (2.3.21) \]

Thus we can apply the theorem of Nevel’son and Has’minskii, where \( Q = Q(\varepsilon, R) \), \( R > \varepsilon > 0 \) is some constant, \( \varepsilon \) is a small enough parameter, \( B_\varepsilon = \{ x \in \mathbb{R}^{N \times M} \text{such that} \| x - \tilde{\omega} \| < \varepsilon \} \) is a spherical neighborhood of the limit point, \( B = \bigcap_{\varepsilon > 0} B_\varepsilon, \ U_\varepsilon(B) = \{ \omega : \rho(\omega, B) < \varepsilon \} \)

\[ V_\varepsilon(B) = \mathbb{R}^{N \times M} \setminus U_\varepsilon(B), \ V_{\varepsilon, B}(B) = V_\varepsilon(B) \cap \{ (\omega(n) : |\omega(n)| < R \} \]

Considering the above statements \((2.3.19, 2.3.20, 2.3.21 \text{ and } 2.3.14)\) we note that the hypothesis of theorem 2.1 are satisfied and so we obtain
\[ P\{ \lim_{n \to +\infty} \inf \rho(\omega(n), B) = 0 \} = 1 \quad (2.3.22) \]

where \( \rho(\omega(n), B) = \inf_{y \in B} \rho(\omega(n), y) \)

Now by \((2.3.22)\) we have that when \( n \to +\infty \) \( \omega(n) \to \tilde{\omega} \) with probability 1.

In fact, since
\[ \lim_{\omega(n) \to \omega} \sup_{n \geq 0} W(n, \omega(n)) = 0 \]

we have
\[ P\{ \lim_{n \to +\infty} W(n, \omega(n)) = 0 \} = 1 \]

Thus we get:
\[ \lim_{n \to +\infty} \omega_i(n) = \tilde{\omega}_i \quad i = 1, ..., N \text{ a.e.} \]

In addition as it has been proven in \((25)\), the algorithm will achieve the given accuracy \( \varepsilon \) within a finite number of updates, that is \( \tau(\varepsilon) < C(\varepsilon) \).

3 Numerical studies

In this section we illustrate our numerical simulations about the convergence of the Kohonen algorithm. First we consider a uniformly distributed data set, then a normal distributed data set, all the data are one dimensional as we already said.

We see that the algorithm does not even converge in mean ( and so also not a.e.) if:

1. \( \eta(n) \), the learning parameter, decreases too fast
2. The neighborhood functions \( \Lambda(i, v) \quad (2.3) \), or \( h(i, v, n) \quad (2.3.4) \) have a range of action too small or too large.

In addition, although the learning parameter and the neighborhood function are optimally chosen, the convergence of the algorithm is slow and it needs a large number of iterations in order to have a good accuracy. So, when the data set is not large enough, it is useful to repeat the presentation of data several times in random order until we have a large data set.

In particular in the case of uniformly distributed data, chosen inside the interval \([0, 1]\), we verify numerically that, having a large data set, choosing any neighborhood function and using as learning parameter \( \eta(n) = \frac{1}{n^\alpha} \) with \( \alpha \geq 1 \) the algorithm does not converge in any sense ( for different initial choices of weights we have different outputs) and the weights are not ordered during the learning procedure . Instead using \( \eta(n) = \frac{1}{n^\alpha} \), with \( \alpha \leq \frac{1}{2} \) we have the convergence in mean. So the convergence property depends on the velocity of decay of \( \eta(n) \). In fact if \( \eta(n) \) decreases too fast, e.g. \( \eta(n) = \frac{1}{n^\alpha} \), with \( \alpha \geq 1 \), the updated weights change their values very little during the learning and so the algorithm is not able to find the final configuration of weights. \( \eta(n) \sim 1/n \) is a too fast decay because after 100 iterations already the variation of the weights is very small and so there is no convergence while \( \eta(n) \sim \frac{1}{\sqrt{n}} \) decreases less quickly ( it assumes values less than 0.01 from \( n > 10^6 \) ) and its velocity of decrease is sufficient to have the convergence.

The choice of \( \eta(n) \) is basic not only for the convergence but also for accuracy. In fact we can have the convergence of the algorithm though the algorithm is not able to identify all the limit weights but only some of them. This happens when the weights are updated too fast in the last part of
the learning procedure or when the range of $\eta(n)$ does not cover all the interval $(0, 1)$, for example when the range of $\eta(n)$ is $(0, 0.5)$. We analyzed the following $\eta(n)$:

1. $\eta(n) = \frac{1}{\sqrt{\log(n)}}$
2. $\eta(n) = \frac{1}{\log(n)}$
3. $\eta(n) = \eta_i \left(1 - \frac{n}{n_{\text{max}}}ight)$
4. $\eta(n) = \frac{1}{\sqrt{n}}$

(where $\eta_i$ and $\eta_f$ are respectively the initial and final value of the function $\eta$ and $n_{\text{max}}$ the maximum number of iterations). For all these cases we have convergence in mean, but for each case there is a different accuracy.

Choosing

1. $\eta(n) = \eta_i (1 - \frac{n}{n_{\text{max}}})$
2. $\eta(n) = \frac{\sqrt{\frac{6 \log(n)}{\sqrt{n}}}}{\sqrt{n} + 1}$

we have convergence a.e. The values of the constants and the particular forms of the functions $\eta(n)$ have been determined for satisfying the constraint $0 \leq \eta(n) \leq 1$. Before explaining the reasons of this statement, we want to discuss the connection of the convergence with the values of the parameters. The choices of the parameters depend on the data distribution. For example for the case 3), in the case of uniformly and normally distributed data, generally we have convergence if we choose $\eta_i$ between 0.1 and 0.9 and $\eta_f$ between $10^{-6}$ and 0.1; in the case 1) of the second list the range of $\eta_i$ is $(0.1, 0.9)$. Instead for example with log-normal distributed data the range of $\eta_i$ is $(0.4, 0.9)$ and of $\eta_f$ is $(0.01, 0.1)$ in the case 3) and in the other case the range of $\eta_i$ is $(0.4, 0.8)$.

After many simulations we saw that there is convergence in mean for $\eta(n)$ such that:

$$\frac{1}{\sqrt{n}} \leq \eta(n) \leq \frac{\sqrt{6 \log(n)}}{\sqrt{n} + 1},$$

instead there is a.e. convergence for $\eta(n)$ such that

$$\frac{\sqrt{6 \log(n)}}{\sqrt{n} + 1} \leq \eta(n) \leq \eta_i (1 - \frac{n}{n_{\text{max}}})$$

The convergence depends also on the values of parameters concerning the neighborhood function.

![Figure 3:](image)

*Figure 3:* On the left we have $\eta(n) = \frac{\sqrt{6 \log(n)}}{\sqrt{n} + 1}$, on the right $\eta(n) = \eta_i (1 - \frac{n}{n_{\text{max}}})$

that is the range of the action of the winner neuron which is determined by $s$ in the case of $\Lambda(i, v)$, and by $\sigma_i$ and $\sigma_f$ in the case of $h(i, v, n)$. The choice of $s$ depends strongly on the number
of weights we fix at the beginning and the number of iterations. For example using a data set of about 10000 uniformly distributed data if we choose \( \eta(n) = \frac{\sqrt{b+\log(n)}}{\sqrt{(n)+1}} \), \( \Lambda(i,v) \) with \( s = 1 \) as neighborhood function and we want to find 30 groups we do not have the convergence (the weights are not ordered) but changing the value of \( s \) conveniently (in this case \( s \geq 2 \)) we obtain the convergence.

If the data set is smaller than 10000, \( s \) is larger than the one of the previous example. In the case of the \( h \) neighborhood function the best choices of \( \sigma_i \) and \( \sigma_f \) are the following:

\[
\begin{align*}
\sigma_i &= \frac{\sqrt{N}}{2} \\
\sigma_f &= 0.01
\end{align*}
\]  
(3.0.23) (3.0.24)

where \( N \) is the number of weights.

We have more than one choice for the parameters to obtain the convergence but different choices give different outputs. We illustrate some examples. Finding out 10 weights for a data set of 10000 uniformly distributed data, using \( \eta(n) = \frac{\sqrt{b+\log(n)}}{\sqrt{(n)+1}} \) and using \( h \) if we choose \( \sigma_i = 20 \) and \( \sigma_f = 0.01 \) the algorithm converges and the range of values of weights is \((0.48,0.50)\), in this case the network identifies 10 different values inside that interval; instead if we choose \( \sigma_i = 5 \) and \( \sigma_f = 0.01 \) the range is \((0.37,0.65)\). We see that the best solution is given by 3.0.23 instead if we choose \( \sigma_i = 5 \) and \( \sigma_f = 0.01 \) the algorithm converges and the range of values of weights is \((0.19,0.82)\). It is important to have the range that covers all the interval of the data set because otherwise we do not find the optimal partition. Since we know that for any data distribution the expectation of weights converges, a small range indicates that the network is able to find only some of the limit values of weights, in fact for the reported example, with \( N = 10 \), we know from [25] that the limit values are: 0.05, 0.15, 0.25, 0.35, 0.45, 0.55, 0.65, 0.75, 0.85, 0.95, so the range of the weights values must be \((0.05,0.95)\), more or less. In the worst choice the network identifies only one limit value. It happens because the range of action is too big; in this case the algorithm updates simultaneously too many weights and they converge to the same value.

An analogous situation happens using \( \Lambda(i,v) \) as a neighborhood function. Using \( \eta(n) = \frac{\sqrt{b+\log(n)}}{\sqrt{(n)+1}} \), searching always 10 weights for a data set of 10000 uniformly distributed data, if we choose \( s \geq 1 \) the algorithm converges but the range of weights values change for different choices of \( s \). Increasing \( s \) the range of weights becomes smaller and the weights converge to the same limit if \( s = 10 \). To be more precise if \( s \) is equal to \( N \), the network generates \( N \) weights (in this case \( N = 10 \)) with the same value. The biggest range, in this case, is obtained with \( s = 1 \). If the number of weights increases the best choice of \( s \) is always the minimum values of \( s \) by which we obtain the convergence of the algorithm. For example in the case we search 50 weights the best choice is \( s = 3 \).

Summarizing to obtain the convergence we must choose \( \eta(n) \) with a convenient monotone decay and with a large range; in addition we must estimate the right parameters of the neighborhood function such that we have convergence and the maximum range for the weights values in order to determine the optimal partition of data set.

As we said previously the error of the expectation of the weights varies for different choices of \( \eta(n) \), and for some choices of \( \eta(n) \) we have a.e convergence. This statement is based on the following analysis: we run the Kohonen algorithm 1000 times for different data sequences. We use at the beginning a set of uniformly distributed data of 4000 elements, then 10000, 20000, 30000, 60000, 120000, 150000 and 250000. This procedure has been done with all the mentioned \( \eta(n) \) and both \( \Lambda \) and \( h \).

At the end of algorithm running for each data set we have 1000 cases of weights limit values. The mean value of these cases actually converges to the centers of the optimal partition of the interval \((0,1)\) for all \( \eta(n) \) and for each neighborhood function. In addition the average error of limit weights, with respect to the exact values of the centers, decreases on increasing the number of iterations for \( \eta(n) = \frac{\sqrt{b+\log(n)}}{\sqrt{(n)+1}} \) and \( \eta_i(1 - \frac{n}{n_{max}}) \) and any neighborhood function; but using \( \Lambda(i,v) \) the error decreases more quickly. Moreover the computing time of the algorithm using \( h \) is about 7 times longer than the one using \( \Lambda \) and the accuracy of weights on the boundaries is worse using \( h \).
The weights near the border are not updated symmetrically and so they are shifted inward by an amount of the order of $\frac{1}{2}N$, where $N$ is the number of weights in the case of $\Lambda(i, v)$ while, using $h$, the weights which are shifted are 4, two for each boundary. Now we illustrate the quoted results. The following tables 1, 2, 3, 4 show the evolution of the error. In the first table there are the average errors of each weight using $\Lambda$ as neighborhood function and 10000 uniformly distributed inputs; instead in the third table there are 60000 uniformly distributed inputs. In the second and in the fourth table it is shown the case of $h$ as neighborhood function. The weights are $N = 10$, so the limit values, which are written in the first column of every tables, are: 0.05, 0.15, 0.25, 0.35, 0.45, 0.55, 0.65, 0.75, 0.85, 0.95

\begin{tabular}{|c|c|c|c|c|c|}
\hline
$\eta_i$ & $\eta_f$ & $\eta_i(1 - \frac{n}{n_{max}})$ & $\sqrt{\frac{6}{\log(n)}}$ & $\sqrt{\frac{\log(n)}{n+1}}$ \\
\hline
0.05 & 0.0561 & 0.0562 & 0.0576 & 0.0559 & 0.0559 \\
0.15 & 0.0189 & 0.0197 & 0.0358 & 0.0088 & 0.0160 \\
0.25 & 0.0239 & 0.0246 & 0.0396 & 0.0183 & 0.0216 \\
0.35 & 0.0185 & 0.0191 & 0.0364 & 0.0104 & 0.0158 \\
0.45 & 0.0202 & 0.0211 & 0.0385 & 0.0104 & 0.0168 \\
0.55 & 0.0189 & 0.0196 & 0.0366 & 0.0107 & 0.0161 \\
0.65 & 0.0198 & 0.0208 & 0.0389 & 0.0111 & 0.0167 \\
0.75 & 0.0238 & 0.0243 & 0.0382 & 0.0185 & 0.0216 \\
0.85 & 0.0180 & 0.0188 & 0.0351 & 0.0089 & 0.0158 \\
0.95 & 0.0555 & 0.0556 & 0.0568 & 0.0558 & 0.0557 \\
\hline
\end{tabular}

Table 1: Mean error of each weight for 10000 iterations using $\Lambda$ as neighborhood function. The $\eta$ are shown in the first row.

\begin{tabular}{|c|c|c|c|c|c|}
\hline
$\eta_i$ & $\eta_f$ & $\eta_i(1 - \frac{n}{n_{max}})$ & $\sqrt{\frac{6}{\log(n)}}$ & $\sqrt{\frac{\log(n)}{n+1}}$ \\
\hline
0.05 & 0.1063 & 0.1061 & 0.1045 & 0.1059 & 0.1061 \\
0.15 & 0.0565 & 0.0564 & 0.0587 & 0.0557 & 0.0562 \\
0.25 & 0.0339 & 0.0342 & 0.0440 & 0.0305 & 0.0325 \\
0.35 & 0.0262 & 0.0267 & 0.0409 & 0.0197 & 0.0238 \\
0.45 & 0.0214 & 0.0222 & 0.0388 & 0.0109 & 0.0183 \\
0.55 & 0.0213 & 0.0223 & 0.0379 & 0.0106 & 0.0185 \\
0.65 & 0.0256 & 0.0264 & 0.0403 & 0.0189 & 0.0232 \\
0.75 & 0.0336 & 0.0343 & 0.0460 & 0.0302 & 0.0322 \\
0.85 & 0.0567 & 0.0570 & 0.0615 & 0.0560 & 0.0566 \\
0.95 & 0.1067 & 0.1069 & 0.1065 & 0.1064 & 0.1068 \\
\hline
\end{tabular}

Table 2: Mean error of each weight for 10000 iterations using $h$ as neighborhood function. The $\eta$ are shown in the first row.

We give some examples to illustrate the error evolution using $\eta(n) = \eta_i(1 - \frac{n}{n_{max}})$ and $\eta(n) = \frac{\sqrt{6\log(n)}}{\sqrt{n+1}}$, the case of a.e. convergence. The tables 5 and 6 concern the application of the algorithm with 4000, 10000, 20000, 30000, 60000, 120000, 150000, 250000 iterations, which are written in the first column, and using $\Lambda$ as neighborhood function. As seen in the tables the error decreases faster using $\eta(n) = \eta_i(1 - \frac{n}{n_{max}})$ and it decreases increasing the iterations; see the figures 4, 5, 6 and figures 7, 8, 9. In some of these pictures there are the histograms of the limit weights values obtained running the algorithm 1000 times for different numbers $M$ of iterations using every time a specific $\eta(n)$. The histograms show
\[
\eta_i \left( \eta f \eta_i \right) \frac{n}{n_{max}} \quad \frac{1}{\log(n)} \quad \frac{1}{\sqrt{\log(n)}} \quad \eta_i \left(1 - \frac{n}{n_{max}}\right) \quad \frac{\sqrt{6+\log(n)}}{\sqrt{n+1}}
\]

| \( \eta_i \left( \eta f \eta_i \right) \frac{n}{n_{max}} \) | \( \frac{1}{\log(n)} \) | \( \frac{1}{\sqrt{\log(n)}} \) | \( \eta_i \left(1 - \frac{n}{n_{max}}\right) \) | \( \frac{\sqrt{6+\log(n)}}{\sqrt{n+1}} \) |
|---|---|---|---|---|
| 0.05 | 0.0565 | 0.0563 | 0.0578 | 0.0560 | 0.0563 |
| 0.15 | 0.0190 | 0.0179 | 0.0342 | 0.0071 | 0.0114 |
| 0.25 | 0.0239 | 0.0234 | 0.0354 | 0.0181 | 0.0189 |
| 0.35 | 0.0199 | 0.0192 | 0.0348 | 0.0079 | 0.0117 |
| 0.45 | 0.0206 | 0.0194 | 0.0365 | 0.0073 | 0.0113 |
| 0.55 | 0.0200 | 0.0189 | 0.0384 | 0.0071 | 0.0114 |
| 0.65 | 0.0188 | 0.0178 | 0.0350 | 0.0079 | 0.0115 |
| 0.75 | 0.0218 | 0.0211 | 0.0343 | 0.0179 | 0.0183 |
| 0.85 | 0.0181 | 0.0170 | 0.0336 | 0.0070 | 0.0108 |
| 0.95 | 0.0556 | 0.0557 | 0.0553 | 0.0560 | 0.0556 |

Table 3: Mean error of each weight for 60000 iterations using \( \Lambda \) as neighborhood function. The \( \eta \) are shown in the first row.

\[
\eta_i(\eta f \eta_i) \frac{n}{n_{max}} \quad \frac{1}{\log(n)} \quad \frac{1}{\sqrt{\log(n)}} \quad \eta_i \left(1 - \frac{n}{n_{max}}\right) \quad \frac{\sqrt{6+\log(n)}}{\sqrt{n+1}}
\]

| \( \eta_i(\eta f \eta_i) \frac{n}{n_{max}} \) | \( \frac{1}{\log(n)} \) | \( \frac{1}{\sqrt{\log(n)}} \) | \( \eta_i \left(1 - \frac{n}{n_{max}}\right) \) | \( \frac{\sqrt{6+\log(n)}}{\sqrt{n+1}} \) |
|---|---|---|---|---|
| 0.05 | 0.1061 | 0.1060 | 0.1040 | 0.1064 | 0.1059 |
| 0.15 | 0.0559 | 0.0558 | 0.0580 | 0.0560 | 0.0555 |
| 0.25 | 0.0326 | 0.0321 | 0.0362 | 0.0302 | 0.0300 |
| 0.35 | 0.0243 | 0.0235 | 0.0340 | 0.0185 | 0.0193 |
| 0.45 | 0.0206 | 0.0196 | 0.0361 | 0.0082 | 0.0125 |
| 0.55 | 0.0215 | 0.0205 | 0.0373 | 0.0088 | 0.0132 |
| 0.65 | 0.0252 | 0.0244 | 0.0356 | 0.0191 | 0.0198 |
| 0.75 | 0.0321 | 0.0317 | 0.0345 | 0.0306 | 0.0299 |
| 0.85 | 0.0548 | 0.0548 | 0.0565 | 0.0562 | 0.0555 |
| 0.95 | 0.1051 | 0.1053 | 0.1045 | 0.1064 | 0.1061 |

Table 4: Mean error of each weight for 60000 iterations using \( h \) as neighborhood function. The \( \eta \) are shown in the first row.

\[
\eta(n) = \eta_i \left(1 - \frac{n}{n_{max}}\right)
\]

| \( \eta(n) = \eta_i \left(1 - \frac{n}{n_{max}}\right) \) | err1 | err2 | err3 | err4 | err5 | err6 | err7 | err8 | err9 | err10 |
|---|---|---|---|---|---|---|---|---|---|---|
| 4000 | 0.0562 | 0.0108 | 0.0183 | 0.0132 | 0.0135 | 0.0144 | 0.0139 | 0.0192 | 0.0110 | 0.0559 |
| 10000 | 0.0559 | 0.0088 | 0.0183 | 0.0104 | 0.0104 | 0.0107 | 0.0111 | 0.0185 | 0.0089 | 0.0558 |
| 20000 | 0.0565 | 0.0083 | 0.0184 | 0.0097 | 0.0089 | 0.0088 | 0.0092 | 0.0179 | 0.0079 | 0.0560 |
| 30000 | 0.0556 | 0.0075 | 0.0180 | 0.0091 | 0.0083 | 0.0082 | 0.0086 | 0.0177 | 0.0073 | 0.0557 |
| 60000 | 0.0560 | 0.0071 | 0.0181 | 0.0079 | 0.0073 | 0.0071 | 0.0079 | 0.0179 | 0.0070 | 0.0560 |
| 120000 | 0.0559 | 0.0065 | 0.0176 | 0.0072 | 0.0060 | 0.0064 | 0.0072 | 0.0180 | 0.0067 | 0.0560 |
| 150000 | 0.0560 | 0.0065 | 0.0180 | 0.0070 | 0.0058 | 0.0060 | 0.0071 | 0.0178 | 0.0065 | 0.0560 |
| 250000 | 0.0560 | 0.0062 | 0.0178 | 0.0067 | 0.0050 | 0.0054 | 0.0069 | 0.0180 | 0.0064 | 0.0562 |

Table 5: Evolution of the mean error for each weight in the case of \( \eta(n) = \eta_i \left(1 - \frac{n}{n_{max}}\right) \). \( err_i \) means: mean error of weight \( i \)

how, increasing \( M \), only in the case of \( \eta(n) = \eta_i \left(1 - \frac{n}{n_{max}}\right) \) and \( \eta(n) = \frac{\sqrt{6+\log(n)}}{\sqrt{n+1}} \) the variance
\[ \eta(n) = \sqrt{6 \log(n)/n+1} \]

| \( \eta(n) = \sqrt{6 \log(n)/n+1} \) | err1 | err2 | err3 | err4 | err5 | err6 | err7 | err8 | err9 | err10 |
|---------------------------------|------|------|------|------|------|------|------|------|------|------|
| 4000                            | 0.0559 | 0.0195 | 0.0233 | 0.0203 | 0.0207 | 0.0210 | 0.0211 | 0.0235 | 0.0198 | 0.0556 |
| 10000                           | 0.0559 | 0.0160 | 0.0216 | 0.0158 | 0.0168 | 0.0161 | 0.0167 | 0.0216 | 0.0158 | 0.0557 |
| 20000                           | 0.0558 | 0.0139 | 0.0204 | 0.0140 | 0.0142 | 0.0140 | 0.0153 | 0.0195 | 0.0131 | 0.0554 |
| 30000                           | 0.0558 | 0.0128 | 0.0190 | 0.0135 | 0.0133 | 0.0128 | 0.0136 | 0.0193 | 0.0129 | 0.0562 |
| 60000                           | 0.0563 | 0.0114 | 0.0189 | 0.0117 | 0.0113 | 0.0114 | 0.0115 | 0.0183 | 0.0108 | 0.0556 |
| 120000                          | 0.0559 | 0.0098 | 0.0177 | 0.0098 | 0.0096 | 0.0098 | 0.0104 | 0.0184 | 0.0100 | 0.0561 |
| 150000                          | 0.0559 | 0.0096 | 0.0182 | 0.0096 | 0.0086 | 0.0088 | 0.0093 | 0.0179 | 0.0089 | 0.0557 |
| 250000                          | 0.0560 | 0.0084 | 0.0179 | 0.0092 | 0.0078 | 0.0081 | 0.0092 | 0.0184 | 0.0089 | 0.0562 |

Table 6: Evolution of the mean error for each weight in the case of \( \eta(n) = \sqrt{6 \log(n)/n+1} \). \( err_i \) means: mean error of weight \( i \).

The histograms tend to 0, each around a limit value of the weight, as we expect since we have a.e. convergence. There are only the histograms for \( \eta(n) = \frac{1}{\log(n)} \) as example of the convergence in mean since the other cases are similar.

The velocity of convergence is very slow after 100000 iterations, it needs many iterations only to change one weight nearer to its limit value; so to construct the histograms with ten columns we need a huge data set. In addition in the pictures with the plot of medium error of each weight we can see that the error decreases always increasing the iterations only in the case of those \( \eta(n) \) which assure the a.e. convergence. Focusing the attention on the pictures of the error we see that from 150000 iterations in the case of \( \eta(n) = \eta_i(1 - \frac{n}{n_{max}}) \) the error decreases very slowly and for the third and eight weight there is a little increase of error \( \sim 0.002 \), it depends on the propagation of the error of the weights from the boundaries.

The a.e. convergence is guaranteed in the case of \( \eta(n) = \eta_i(1 - \frac{n}{n_{max}}) \) and \( \eta(n) = \frac{\sqrt{6 \log(n)}}{\sqrt{n+1}} \) by the monotonically decrease of standard deviation of weights as the figures 10 and 11 show.
Figure 5: Histograms in the case of $\eta(n) = \frac{\sqrt{6+\log(n)}}{\sqrt{n+1}}$, uniformly distributed data and for different numbers $M$ of iterations.

Figure 6: Histograms in the case of $\eta(n) = \frac{1}{\log(n)}$, uniformly distributed data and for different numbers $M$ of iterations.

Similar results are obtained with the normally distributed data but for a special choice of the learning parameter. In fact our theorem does not hold for gaussian distribution as we already mentioned.

Also in this case we have convergence in mean with all the $\eta$ and for any neighborhood function; and convergence a.e for $\eta(n) = \eta_i(1 - \frac{n}{n_{\text{max}}})$ and $\eta(n) = \frac{\sqrt{6+\log(n)}}{\sqrt{n+1}}$.

We show in the following histograms (figures 12, 13) and plots (figures 14, 15) only the results for a.e convergence:
Figure 7: Plot of the mean error for each limit weight in the case of $\eta(n) = \eta_i \left(1 - \frac{n}{n_{\text{max}}} \right)$ and uniformly distributed data. The numbers on the x axes indicate the following iterations: 4000, 10000, 20000, 30000, 60000, 120000, 150000, 250000.

Figure 8: Plot of the medium error of each limit weight in the case of $\eta(n) = \sqrt{\frac{n}{\log(n)}} \sqrt{n+1}$ and uniformly distributed data. The numbers on the x axes indicate the following iterations: 4000, 10000, 20000, 30000, 60000, 120000, 150000, 250000.

Before explaining our application of Kohonen algorithm to microarrays data, we make some remarks on the repetitions of data set presented to the network. This procedure is necessary because the data set is small for microarray data. The accuracy improves by increasing the number of samples and this technique does not change the limit if there is the almost everywhere convergence.

To be sure we have done the same analysis shown above with a data set of 2000 elements repeated
Figure 9: Plot of the medium error of each limit weight in the case of $\eta(n) = \frac{1}{\log(n)}$ and uniformly distributed data. The numbers on the x axes indicate the following iterations: 4000, 10000, 20000, 30000, 60000, 120000, 150000, 250000.

Figure 10: The standard deviation of the weights in the case of $\eta(n) = \eta_i(1 - \frac{n}{n_{\text{max}}})$ and uniformly distributed data. The numbers on the x axes indicate the following iterations: 4000, 10000, 20000, 30000, 60000, 120000, 150000, 250000.

at the beginning 2 times, then 5, 10, 15, 30, 60 and 125 so to have the same iterations of the previous analysis. The results are similar, that is we have a.e. convergence for the previous case of $\eta(n)$, that is:

- $\eta(n) = \eta_i(1 - \frac{n}{n_{\text{max}}})$
- $\eta(n) = \frac{\sqrt{2 \times \log(n)}}{\sqrt{n+1}}$
Figure 11: The standard deviation of the weights in the case of $\eta(n) = \sqrt{\frac{6\log(n)}{\sqrt{n+1}}}$ and uniformly distributed data. The numbers on the x axes indicate the following iterations: 4000, 10000, 20000, 30000, 60000, 120000, 150000, 250000.

Figure 12: Histograms in the case of $\eta(n) = \eta_i(1 - \frac{n}{n_{max}})$ and normal distributed data and for different numbers $M$ of iterations

We show the histograms [16][17] in these two case to illustrate this statement:

4 Application to microarrays data

In this section we show how we have applied the Kohonen network to micro-arrays data set. Following our strategy we have made the cluster analysis of the data for each sample and compared the genes appearing in the nearby clusters, in this way we exploit the neat convergence properties
Figure 13: Histograms in the case of $\eta(n) = \frac{\sqrt{6+\log(n)}}{\sqrt{n}+1}$, normal distributed data and for different numbers $M$ of iterations.

Figure 14: The standard deviation of the weights in the case of $\eta(n) = \eta_i(1 - \frac{n}{n_{\text{max}}})$ and normal distributed data. The numbers on the x axes indicate the following iterations: 4000, 10000, 30000, 60000, 90000, 150000, 250000, 350000.

...of the one-dimensional case. The set of data we analyzed is the same as the one published in [30] where there is an exhaustive description of microarrays sample preparation. In brief total RNA (ttrRNA) was extracted and purified from mammary glands in control and transgenic mice. ttrRNA were pooled to obtain three replicates for the mammary glands of 2-week-pregnant WT BALB/c mice (wk2prg), of 22 week old untreated BALB-neuT mice (wk22nt), and of 22 week old primed and boosted BALB-neuT mice (wk22pb) and two replicates for the mammary glands of 10 week old untreated BALB-neuT mice (wk10nt). Chips were scanned to generate digitized image...
Figure 15: The standard deviation of the weights in the case of $\eta(n) = \sqrt{6 \times \log(n) + n + 1}$ and normal distributed data. The numbers on the x axes indicate the following iterations: 4000, 10000, 30000, 60000, 90000, 150000, 250000, 350000.

Figure 16: Histograms in the case of $\eta(n) = \eta_i (1 - \frac{n}{n_{max}})$ and uniformly distributed data and for different numbers $M$ of iterations obtained repeating the data several times.

data (DAT) files.
DAT files were analyzed by MAS 5.0 to generate background- normalized image data (CEL files). Probe set intensities were obtained by means of the robust multi array analysis method ([4]). The full data set was normalized according to the invariant set method. The full-shaped procedure described by Saviozzi et al ([29]) was then applied. The resulting 5482 probe sets were analyzed by combining two statistical approaches implemented in significance analysis of micro-arrays ([3]): two classes unpaired sample method and the multi classes response test. This analysis produced...
Figure 17: Histograms in the case of \( \eta(n) = \frac{\sqrt{6 + \log(n)}}{\sqrt{n} + 1} \) and uniformly distributed data and for different numbers \( M \) of iterations obtained repeating the data several times.

A total of 2179 probe sets differentially expressed in at least one of the three experimental groups. The 2179 probe sets were converted in virtual two dye experiments comparing all replicates of each experimental groups with index \( j = 1, 2, 3 \) (i.e., \( \omega_{k22nt_i}, \omega_{k22nt_{i+1}}, \omega_{k22nt_{i+2}} \), \( i = 1, 2, 3 \)). Therefore we have 3 replicates of 8 experimental groups.

We apply the Kohonen algorithm to the 2179 probe sets. Our main aim is to detect which genes are up-modulated in \( \omega_{k22pb} \) respect to \( \omega_{k22nt} \) and \( \omega_{k10nt} \).

The first step is to implement the one dimensional Kohonen algorithm in Matlab and study its convergence putting inside as inputs data the 2179 expression levels of genes of any experimental group. In particular our set contains the log values of expression levels of genes, which are normally distributed in any experimental group; so, with regard the numerical studies done, we choose \( \eta_i \approx \frac{1}{\sqrt{\log(n)}} \), with \( \eta_i = 0.8 \) because we have the almost everywhere convergence, and \( \Lambda \) as neighborhood function, since we have the best accuracy in this case.

For each experimental group the input set \( \Omega \) is only of 2179 elements so to improve the accuracy we repeat the data presentation set several times in different order. We present the data set 100 times, in such way the input set is almost 220000 patterns; in this case the mean error of weights is about 0.01 (as we have seen in our previous studies) and since the average variability of the expression levels of genes among the replicates is about 0.133, this error is acceptable.

We run the Kohonen algorithm fixing \( N \), the number of weights, equal to 30 and then we choose among the limit values found only those weights with a distance greater than two times the average variability of the expression levels of genes among the replicates. We select the weights in this way because otherwise the assignment of a gene to a particular cluster could be not unique. The choice of \( N = 30 \) has been done analyzing the distribution of the data and considering the variability of the expression levels of genes among the replicates. To obtain weights with a distance greater than two times the average variability of genes expressions we can fix also \( N = 15 \), but in this way we lose precision in finding weights at the boundaries of the data set interval. It happens because the data are normally distributed, therefore they are concentrated near the mean of the data set and more we move away from mean more the distance between weights increases, therefore it is better choosing more weights than those which have an optimal distance between them, such that it is possible to detect more weights at boundaries, since we want to find out up-modulated genes.

Once we have found the limit weights values we separate the data into the identified clusters. This procedure has been done for every experimental group indexed by \( j \) (\( \omega_{k10nt_i}, \omega_{k22nt_{i+1}}, \omega_{k22nt_{i+2}} \), \( i = 1, 2, 3 \)).
wk22nt, wk22pb, wk22prg, i = 1, ..3), so we have eight classifications for each replicate. In addition we choose one of the 24 (8 for each replicate) sequences of limit weights and we separate the data of every experimental into the clusters identified by the chosen sequence. In this way we obtained 24 classifications for every sequence of limit weights (that are 24).

Once we have obtained these classifications we improve the precision of assignment of genes considering their biological variability; therefore we have checked if the expression level of genes which lay on the boundaries of a cluster can be considered really belonging to that cluster or, because its variability, to its neighbor. In detail, if the expression of the genes, incremented of its biological error, is closer to the weight of its cluster than to its nearest weight, the assignment of the gene does not change, otherwise the gene is assigned to the cluster corresponding to its nearest weight.

We can observe that, since the limit weights are ordered, the clusters, with which they are associated can be ordered in ascending way. Therefore in clusters related to high index we find genes with a greater expression level than in clusters with low index.

For each replicates we select only those genes that are in clusters with high index for the classifications obtained respect the limit weights found analyzing the data of wk22pb, wk22prg, i = 1, ..3 and in low clusters for classifications obtained by means of the limit weights found analyzing the data of wk10nt, wk22nt, j = 1, 2. After this procedure we have identified a set of 70 up-modulated genes in wk22pb respect to wk22nt and wk10nt. Among these genes there are 25 ones that have not been found by Quaglino et al. These new genes found are shown in the table 7.

5 Conclusion

We have improved the theorem on the a.e. convergence of the Kohonen algorithm because we prove the sufficiency of a slow decay of the learning parameter, \( \sum \eta(n) = \infty \), similar to the one used in the applications. The theorem is not complete because we are not able to prove the necessity of such condition and future work should be concentrated on this point. But for doing such a research one has to find something functional more similar to the Liapunov functional than the one currently available. This could make it possible using some argument of convergence similar to the one used for the simulated annealing. We made also many numerical simulations of convergence in order to find the choice of \( \eta(n) \) which minimizes the rate of decrease of the average error and also for finding which version of the learning algorithm is better to use. We found that the optimal choice is:

\[
\frac{\sqrt{6 \ast \log(n)}}{\sqrt(n) + 1} \leq \eta(n) \leq \eta_i (1 - \frac{n}{n_{\text{max}}})
\]

The algorithm with \( \Lambda \) neighborhood function is better than the one using the function \( h \) since it has bad convergence properties. The latter one is commonly used in the simulations. After this detailed analysis we applied our optimal choice to the genetic expression levels of tumor cells. The 25 genes identified by us were also consistent with the biological events investigated by Quaglino (30).
| Affymetrix ID | Gene Title                                                                 | Gene Symbol |
|--------------|---------------------------------------------------------------------------|-------------|
| 100376_f_at  | similar to immunoglobulin heavy chain                                     | LOC432710  |
| 101720_f_at  | immunoglobulin kappa chain variable 8 (V8)                               | Igk-V8      |
| 101743_f_at  | immunoglobulin heavy chain 1a (serum IgG2a)                              | Igh-1a      |
| 101751_f_at  | gene model 194, (NCBI)                                                    | Gm194       |
|              | gene model 189, (NCBI)                                                    | Gm189       |
|              | gene model 192, (NCBI)                                                    | Gm192       |
|              | gene model 1068, (NCBI)                                                   | Gm1068      |
|              | gene model 1069, (NCBI)                                                   | Gm1069      |
|              | gene model 1418,(NCBI)                                                   | Gm1418      |
|              | gene model 1419, (NCBI)                                                   | Gm1419      |
|              | gene model 1499, (NCBI)                                                   | Gm1499      |
|              | gene model 1502, (NCBI)                                                   | Gm1502      |
|              | gene model 1524, (NCBI)                                                   | Gm1524      |
|              | gene model 1530, (NCBI)                                                   | Gm1530      |
|              | similar to immunoglobulin light chain variable region                     | LOC434586  |
|              | similar to immunoglobulin light chain variable region immunoglobulin light chain variable region gene model 1420, (NCBI) | LOC458448  |
| 102722_g_at  | expressed sequence AI324046                                              | AI324046    |
| 103990_at    | FBJ osteosarcoma oncogene B                                               | Fosb        |
| 104638_at    | ADP-ribosyltransferase 1 Art1                                             |             |
| 160927_at    | angiotensin I converting enzyme (peptidyl-dipeptidase A) 1               | Ace         |
| 161650_at    | secretory leukocyte peptidase inhibitor                                   | Slpi        |
| 162286_r_at  | Fc fragment of IgG binding protein                                        | Fcgbp       |
| 92737_at     | interferon regulatory factor 4                                            | Irf4        |
| 92858_at     | secretory leukocyte peptidase inhibitor                                   | Slpi        |
| 93527_at     | Kruppel-like factor 9                                                     | Klf9        |
| 94442_s_at   | G-protein signalling modulator 3 (AGS3-like, C. elegans)                  | Gpsm3       |
| 94725_f_at   | similar to immunoglobulin light chain variable region                     | LOC43033    |
| 96144_at     | inhibitor of DNA binding 4                                                | Id4         |
| 96963_s_at   | immunoglobulin light chain variable region                                | 8-30        |
| 96975_at     | immunoglobulin kappa chain variable 1 (V1)                               | Igk-V1      |
|              | Ig kappa chain                                                            | IgM         |
|              | immunoglobulin kappa chain variable 5 (V5family)                         | Igk-V5      |
|              | immunoglobulin light chain variable region                               | bl1         |
| 97402_at     | indoleethylamine N-methyltransferase                                      | Inmt        |
| 97826_at     | Fc fragment of IgG binding protein                                        | Fcgbp       |
| 98452_at     | FMS-like tyrosine kinase 1                                                | Fit1        |
| 98765_f_at   | similar to immunoglobulin heavy chain                                     | LOC382653   |
|              | similar to immunoglobulin heavy chain constant region                     | LOC544903   |
| 99850_at     | Immunoglobulin epsilon heavy chain constant region                       |             |
| 102156_f_at  | immunoglobulin kappa chain constant region                               |             |
|              | immunoglobulin kappa chain variable 21 (V21)                             |             |
|              | immunoglobulin kappa chain similar to anti-glycoprotein-B of human      |             |
|              | Cytomegalovirus immunoglobulin V1 chain                                   |             |
|              | immunoglobulin kappa chain similar to anti-PRSV coat protein             |             |
|              | monoclonal antibody PRSV-L 3-8                                           |             |
|              | immunoglobulin light chain variable region                               |             |
| 98475_at     | matrilin 2                                                                | Matn2       |

Table 7: The up modulated genes found out
References

[1] M.R. Anderberg, *Cluster Analysis for applications* Accademic Press, New York and London, (1973).

[2] P. Tamayo, D. Slonim, J. Mesirov, Q. Zhu, S. Kitareewan, E. Dmitrovsky, E.S. Lander, *Interpreting patterns of gene expression with self-organizing maps: Methods and application to hematopoietic differentiation*, Proc. Natl. Acad. Sci. USA, Vol. 96, 2907-2912, (1999).

[3] V.G. Tusher ET AL, *Significance analysis of micro-arrays applied to the ionising radiation response*, Proc. Natl. Acad. Sci. USA, Vol. 98, 5116-5121, (2001).

[4] R.A. Irizarry ET AL, *Summaries of Affymetrix GeneChip probe level data*, Nucleic Acids Res., Vol.31, (2003).

[5] M. Eisen, P.T. Spellman, P.O. Brown, D. Botstein, *Cluster analysis and display of genome-wide expression patterns*, Proc. Natl. Acad. Sci. USA, Vol.95, 14863-14868, (1998).

[6] T. Kohonen, *Self-Organization and Associative Memory Process*,Springer-Verlag, Berlin,(1989).

[7] T. Kohonen, *Analysis of a Simple Self-Organizing Process*, Biological Cybernetics, Vol.44, 135–140, (1982).

[8] T. Kohonen, *Self-Organizing maps: optimization approaches*, Artificial Neural Networks, Vol.1, 891–990, (1991).

[9] J. Hertz, A. Krogh, R. Palmer, *Introduction to the theory of neural computation*, Lectures Notes of Santa Fe Institute, Addison Wesley, (1991) Biological Cybernetics.

[10] M.Shcherbina, B.Tirozzi, The Free Energy of a Class of Hopfield Models. J. of Stat. Phys., 72 1/2, 113-125 (1993)

[11] M.Shcherbina, B.Tirozzi. Rigorous Solution of the Gardner Problem. Comm. Math. Phys., 234, 383-422 (2003)

[12] M.Mezard, G.Parisi, M.A.Virasoro: Spin Glass Theory and Beyond. Singapore: World Scientific, 1987

[13] Z-P. Lo e Bavarian, *On the rate of convergence in topology preserving neural networks* Biological Cybernetics, Vol.65 55–63, (1991).

[14] C.Bouton, G.Pages, *Self-organization and a.s. convergence of the one-dimensional Kohonen algorithm with non uniformly distributed stimuli* Stochastic Process Appl, Vol.47 249–274, (1993).

[15] M. Cottrell and J. C. Fort, *Etude d’un processus d’auto-organisation* Annales de l’Institut Henri Poincar, Vol.23 1–20, (1987).

[16] Ed. Erwin, K. Obermayer, K. Schulten, *Self-Organizing maps: stationary states, metastability and convergence rate*, Biological Cybernetics, Vol.67, 35–45, (1992).

[17] Ed. Erwin, K. Obermayer, K. Schulten, *Self-Organizing maps: Ordering, convergence properties and energy function*, Biological Cybernetics, Vol.67, 47–55, (1992).

[18] J.C. Fort, G.Pages, *On the a.s. convergence of the Kohonen algorithm with a general neighborhood function*, The Annals of Applied Probability, Vol.5, 1177–1216, (1995).

[19] Siming Lin, Jennie Si, Weigh Value Convergence of the SOM Algorithm for discrete input, Neural Computation, Vol.10, 807–814, (1998).

[20] M.B. Nevel’son and R.Z.Has’minskii, *Stochastic Approximation and Recursive Estimation*, Translation of Math. Monograph 47, Amer.Math.Soc, Providence,RI, (1976 ).

[21] H. Ritter, K. Shulten , *On the stationary states of Kohonen’s Self-Organizing Sensory Mapping*, Biological Cybernetics, Vol.54, 99–106, (1986).

[22] H. Ritter, K. Shulten, *Kohonen’s Self-Organizing maps: Exploring their computational capabilities*,Proceedings of the ICNN’88, IEEE International Conference on Neural Networks, Vol 1, 109–116, (1988).
[23] Ali A. Sadeghi, *Convergence in distribution of the multidimensional Kohonen algorithm*, Journ. of Appl. Prob., Vol.38, 136–151, (2001).

[24] J.G. Taylor, M. Budinich, *On the ordering conditions for self-organising maps*, preprint.

[25] J.F. Feng, B. Tirozzi, *Convergence Theorem for the Kohonen Feature mapping Algorithms with VLRPs*, Computer Math. Applic., Vol.33 No.3, 45–63, (1997).

[26] V.V. Tolat, *An analysis of Kohonen’s self-organizing maps using a system of energy functions*, Biological Cybernetics, Vol.64, 155–164, (1990).

[27] J. Vesanto, E. Alhoniemi, *Clustering of the Self-Organizing Map*, IEEE Transactions on Neural Networks, Vol. 11, Issue 3, 586–600, (2000).

[28] H. Yin, N.M. Allison, *On the distribution and convergence of feature space in self-organizing maps*, Neural Computation, Vol. 7, 1178–1187, (1995).

[29] S. Saviozzi et al, *Microarrays data analysis and mining*, Methods in molecular medicine, Vol.94, 67–90, (2003).

[30] E. Quaglino, R. Calogero, *Concordat morphologic and gene expression data show that a vaccine halts HER-2/neu preinvasive lesions*, The Journal of Clinical Investigation, Vol.113, No.5, (2004).