GRID distribution supporting chaotic map clustering on large mixed microarray data sets

Angelica Tulipano INFN, Section of Bari

Andreas Gisel ITB - CNR, Section of Bari

Information Society and Media

Microarray data

- **Microarray data contain the expression values of thousands of genes**
- **This allows to detect the collective cell behaviors**
- **Genes with similar temporal and spatial gene expression patterns are believed to be governed by a common regulatory logic**

- **Hundreds of experiments with the same array design are available**

➔ comparing expression levels over a wide range of experiments can reveal new and valuable information about behaviours of genes.

Microarray data

We selected 587 data sets covering 24 biological experiments from a collection of experiments of the Affimetrix microarray 'Human Genome U133 Array Set HG-U133A' related to 22215 genes.

Data have been organized in an expression matrix $D = n_g \times n_s$, where n_g (=22215) is the number of genes and n_s (=587) is the number of samples (experiments).

Clustering

To analyse the data, having no *a priori* knowledge on their structure, e.g. the number of classes or the geometric distribution, we have chosen an unsupervised hierarchical clustering algorithm based on the cooperative behaviour of an inhomogeneous lattice of coupled chaotic maps, the Chaotic Map Clustering (CMC)[1]

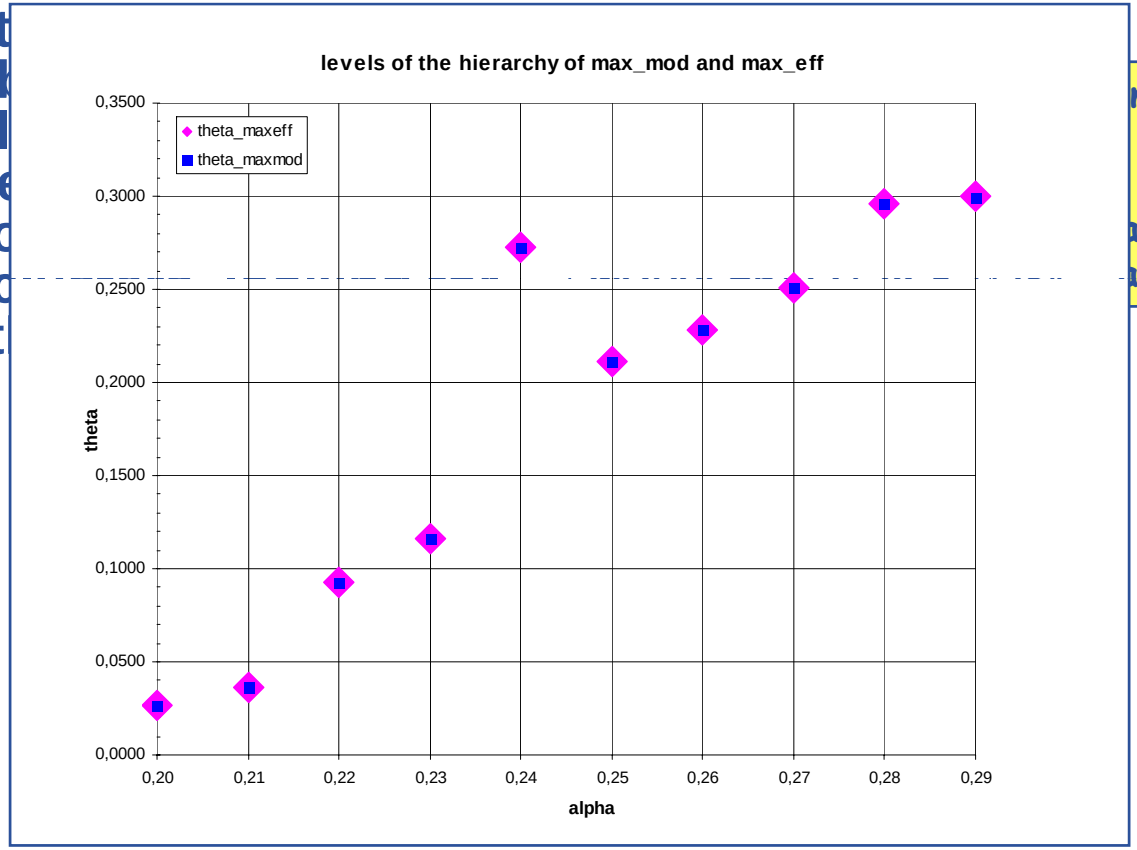
[1] L. Angelini, F. De Carlo, C. Marangi, M. Pellicoro and S. Stramaglia, *Clustering Data by Inhomogeneous Chaotic Map Lattices,* Phys. Rev. Lett., Vol. 85, No. 3, pp 554-557 (2000).

Chaotic Map Clustering

- CMC does not utilize the distances directly for data partitioning, but it generates "chaotic" trajectories by assigning a dynamical variable (i.e. a chaotic map) to each data point.
- Pairs of maps are then coupled by means of a decreasing function of the distance of the corresponding data points.
- The mutual information between pairs of maps, in the stationary regime, is then used as the similarity index for clustering the data set.
- By setting different threshold values for the mutual information, a hierarchical partition of the data can be obtained as a tree of clusters.

Control of the clustering partition

To choose t
of the data b
hierarchical
CMC we use
a measure o
division in c
its peak in t



nts of cluster i and

elements of cluster i

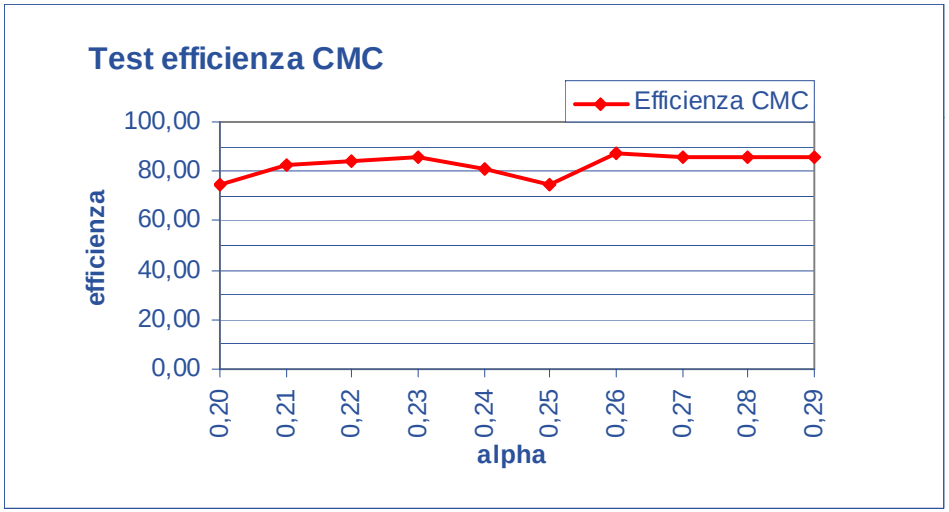
$a_i a_j$

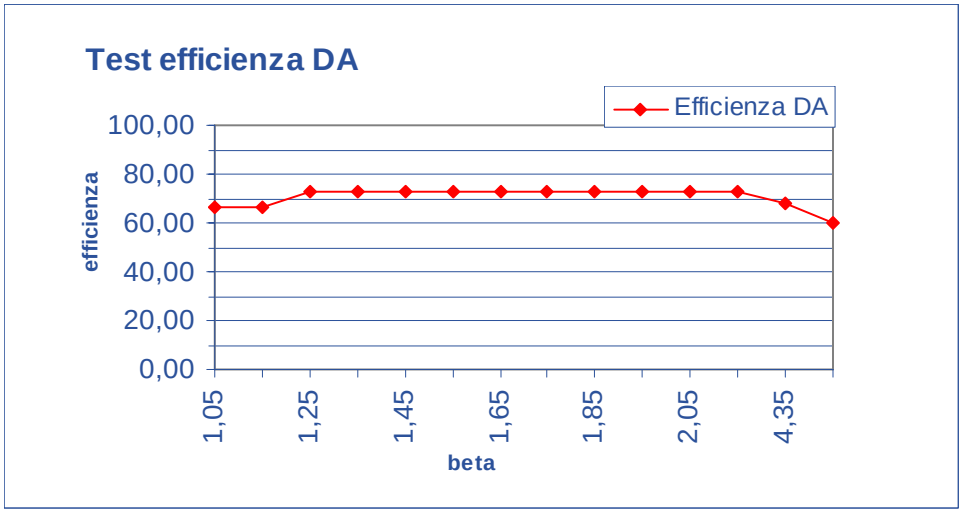
a_i^2)

[4] Khan J, et al. *Classification and diagnostic prediction of cancers using gene expression profiling and artificial neural networks*, Nat. Med. , Vol. 7, No. 6, pp 673-679 (2001)..

Efficiency of CMC

Comparison between CMC and Deterministic Annealing (DA).



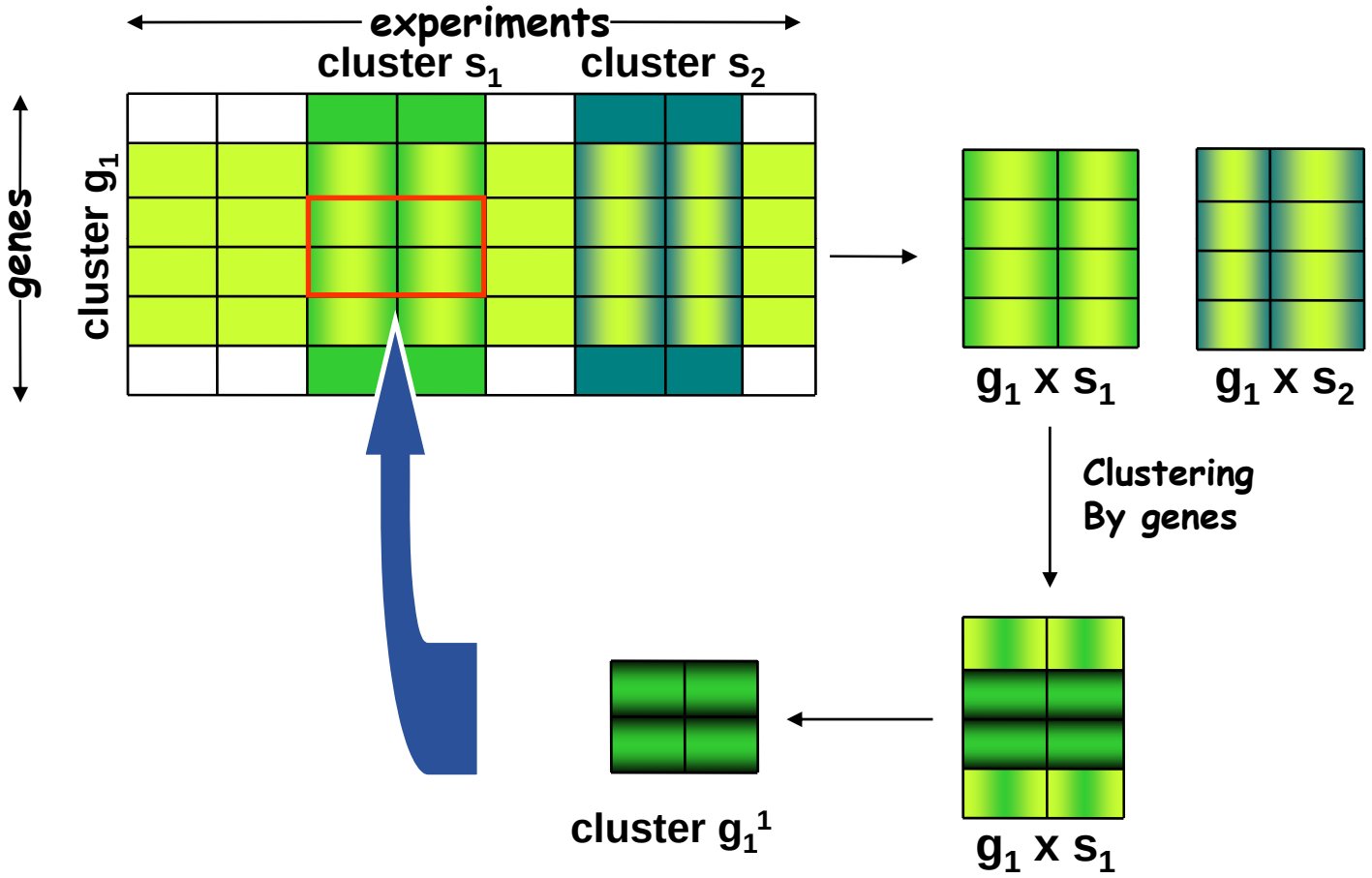


Maximal efficency of

- CMC ➔ 87%
- DA ➔ 73%

Coupled two way clustering

By focusing on small subsets, we lowered the noise induced by the other samples and genes



[8] Getz, G., Levine, E., Domany, E., (2000a) Coupled two-way clustering analysis of gene microarray data. *Proc. Natl. Acad. Sci. USA* **97**, 12079-12084

Cluster validation

Cluster validation method based on resampling[5]:

a cross-validation procedure where subsets of the data under investigation are constructed randomly, and the cluster algorithm is applied to each subset

Connectivity matrix for each resampled matrix

$$Tij = \begin{cases} 1 & \text{points } i \text{ and } j \text{ belonging to the same cluster} \\ 0 & \text{otherwise} \end{cases}$$

Those were compared to the connectivity matrix of the original matrix

Starting from the overlap[6] of the original and resampling connectivity matrices we can define "sensitivity", "positive predictive value" and "specificity", useful quality measures of a clustering result.

[5] Levine E. and Domany E., *Resampling method for unsupervised estimation of cluster validity*, Neural Comp. , Vol. 13, pp 2573-2593, (2001).
[6] Van deer Laan, M.J., Bryan, J., *Gene espression analysis with the parametric bootstrap*, Biostatistics, Vol. 2, No. 4: pp 445-461, (2001).

Problems of resampling

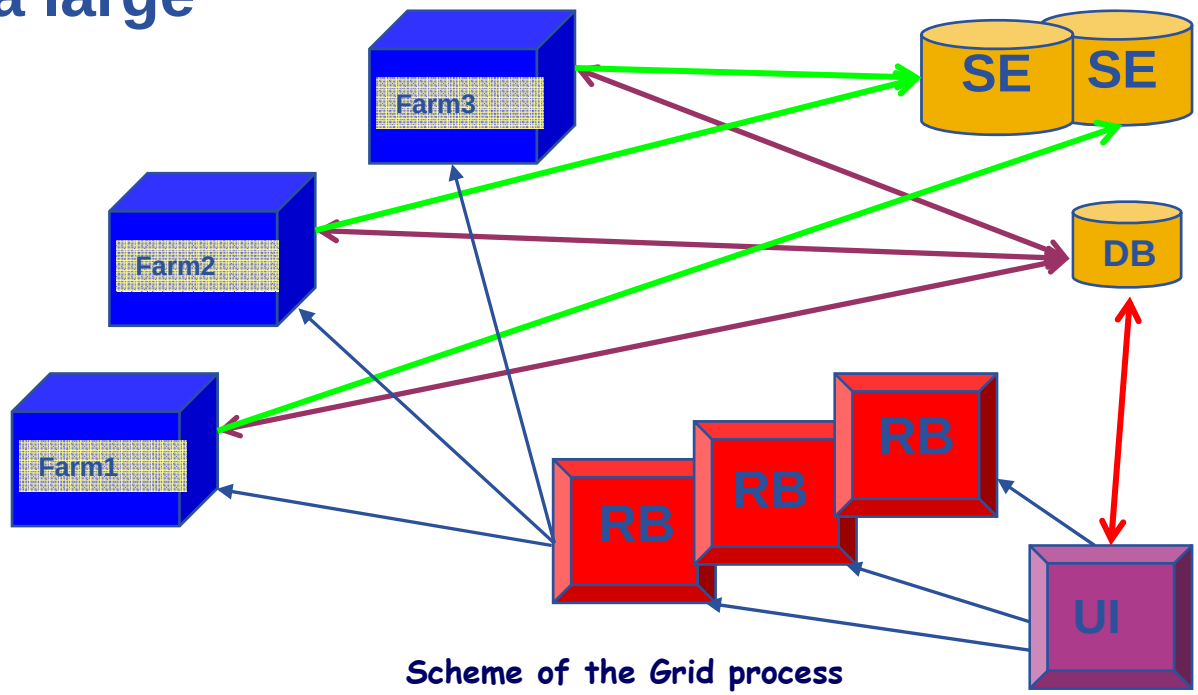
To validate the partition we have obtained by applying CMC to the original matrix 22215x587, we generated 50 randomly resampled matrices 16661x587

PROBLEM

- **clustering a single matrix of such a size takes about 2 hours;**
- **clustering the whole set of resampled matrices would totally occupy one single CPU for about 4 days.**

Grid distribution

A job submission tool[7] was used for the submission of a large number of jobs



Scheme of the Grid process

[7] http://webcms.ba.infn.it/cms-software/index.html/index.php/Main/JobSubmissionTool

Results I

The entire set of matrices was analysed using 59 worker nodes of the EGEE infrastructure within the Biomed VO

Some statistics about the distribution
- 59 jobs on 59 worker nodes:
- 50 succesfull
- 4 failed
- 5 stopped (64 bit)

3 hours of running (due to queue of the worker nodes)

The clustering process of a matrix of such size is very intensive, occupying more than 1.5 GB of RAM and this is a requirement which not all the worker nodes have.

Results II

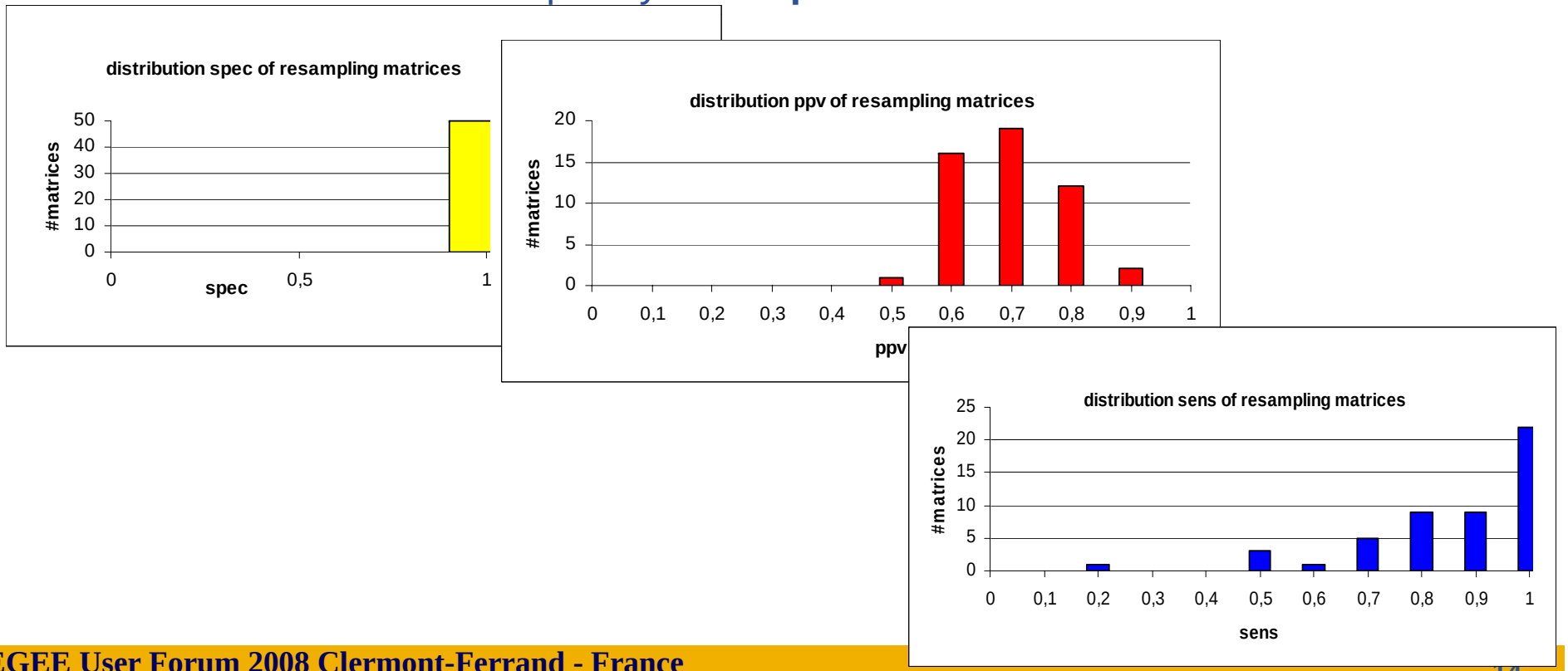
The average value of

the specificity is 0.95

the positive predicted value is 0.65

the sensitivity is 0.81

- **these results** validate **our clusters**
- **but also reflect the** complexity **of the problem here considered**



Conclusion

- Using the GRID infrastructure we are able to validate efficiently and accurately large amount of evaluated clusters
- We demonstrated that CMC is a potential clustering algorithm for large and heterogeneous microarray data

- We demonstrated a application where we clearly differentiated when to use the GRID infrastructure and when to use local resources

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andreas.gisel@ba.itb.cnr.it

Thank you for your ATTENTION!!