An Intelligent Agents Architecture for DNA-microarray Data Integration

Mauro Angeletti, Rosario Culmone and
Emanuela Merelli

Università di Camerino

NETTAB
Genova, 17 May 2001

NETTAB 2001

University of Camerino

Outline

- Motivations
- Main choices in the system - IMAB
- System's architecture
- Mobile agent model
- Preliminary results
- On-going work

Motivations

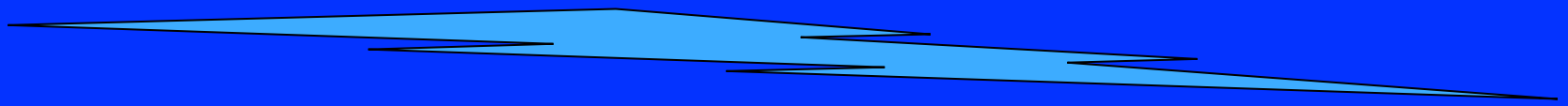
- Electronic diagnostic tool = diagnosis
  - Significant amount of data (ORFs, Experiments, …) disseminated and duplicated in a myriad of different dbs and repositories
  - Different access modes
  - Several actors (researchers, doctors, …)
  - …
- Our-goal:
  - define a general platform IMAB (Intelligent Mobile Agent platform for Biological data) to support "genetic data analysis"
  - define a declarative language IMABL to specify agents

What is an agent?

An agent is a program capable of acting autonomously in order to accomplished tasks on behalf of its user

- There are several dimensions to classifying existing software agents:
  - *mobility, ability, reactivity …*
- In our context, an agent is a program that can move between nodes by preserving the status and managing information (i.e. knowledge) useful to perform its *mission*

Main choices



Chioce 1: all XML

- It's a W3C standard for data transfer
- Many tools are or will be available
- It's easy to use
- ...

- Bio data DTDs are under definition

Chioce 2: all declarative

- Fast deployment
- Easy administration
  - λ e.g., dynamic change of rules, experiment categories …
- Automatic verification
  - λ e.g., correctness of protocols
  - λ e.g., fairness of an extraction system
- etc.

Chioce 3: all autonomous

- Each node is an autonomous elaborative unit
- Each node can have its operating system
- Each node can have a DBMS and/or XML repository

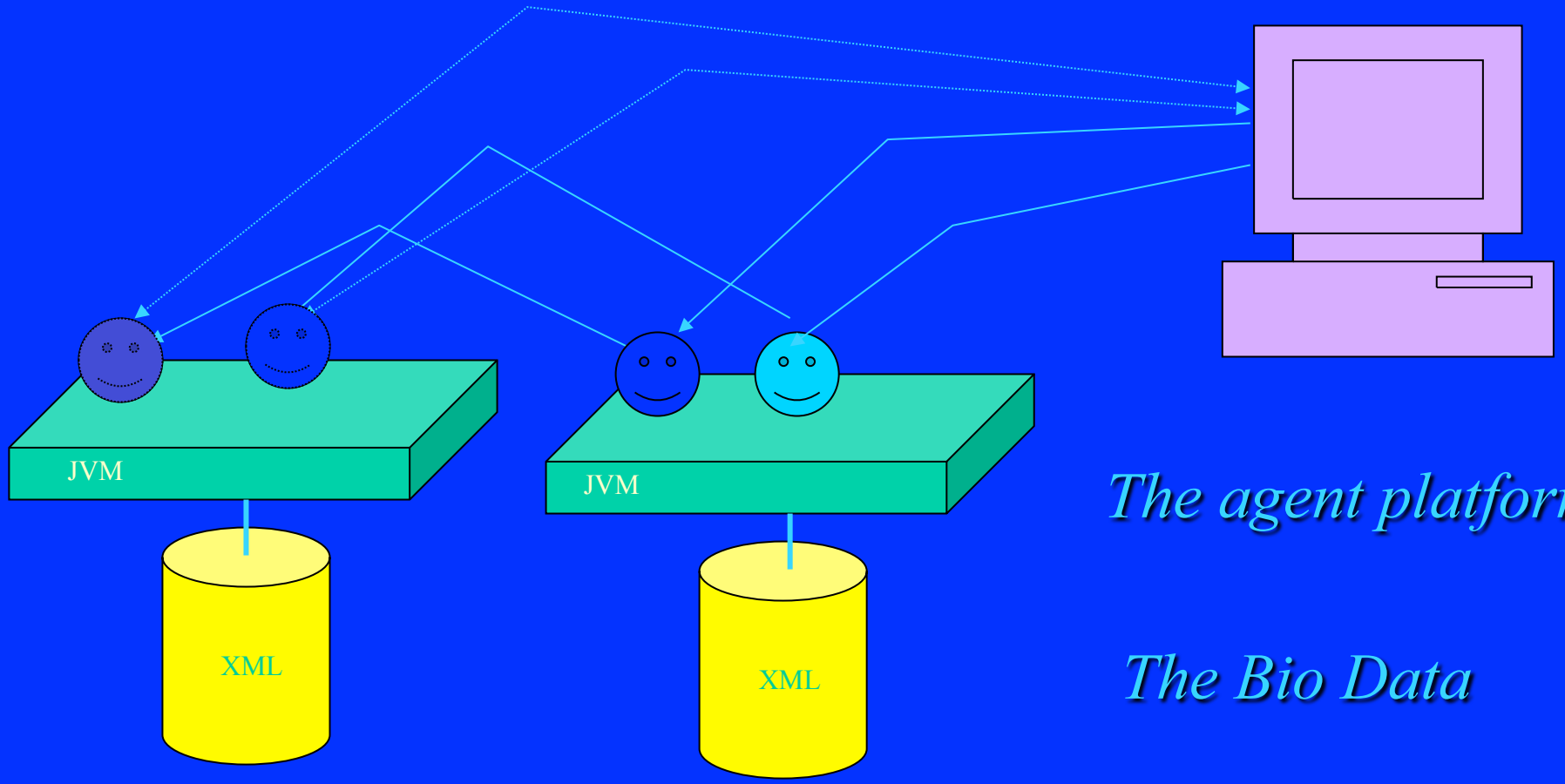
Choice 4: all JVM

- Each node must have a JVM

How it works …

Single agent

The People

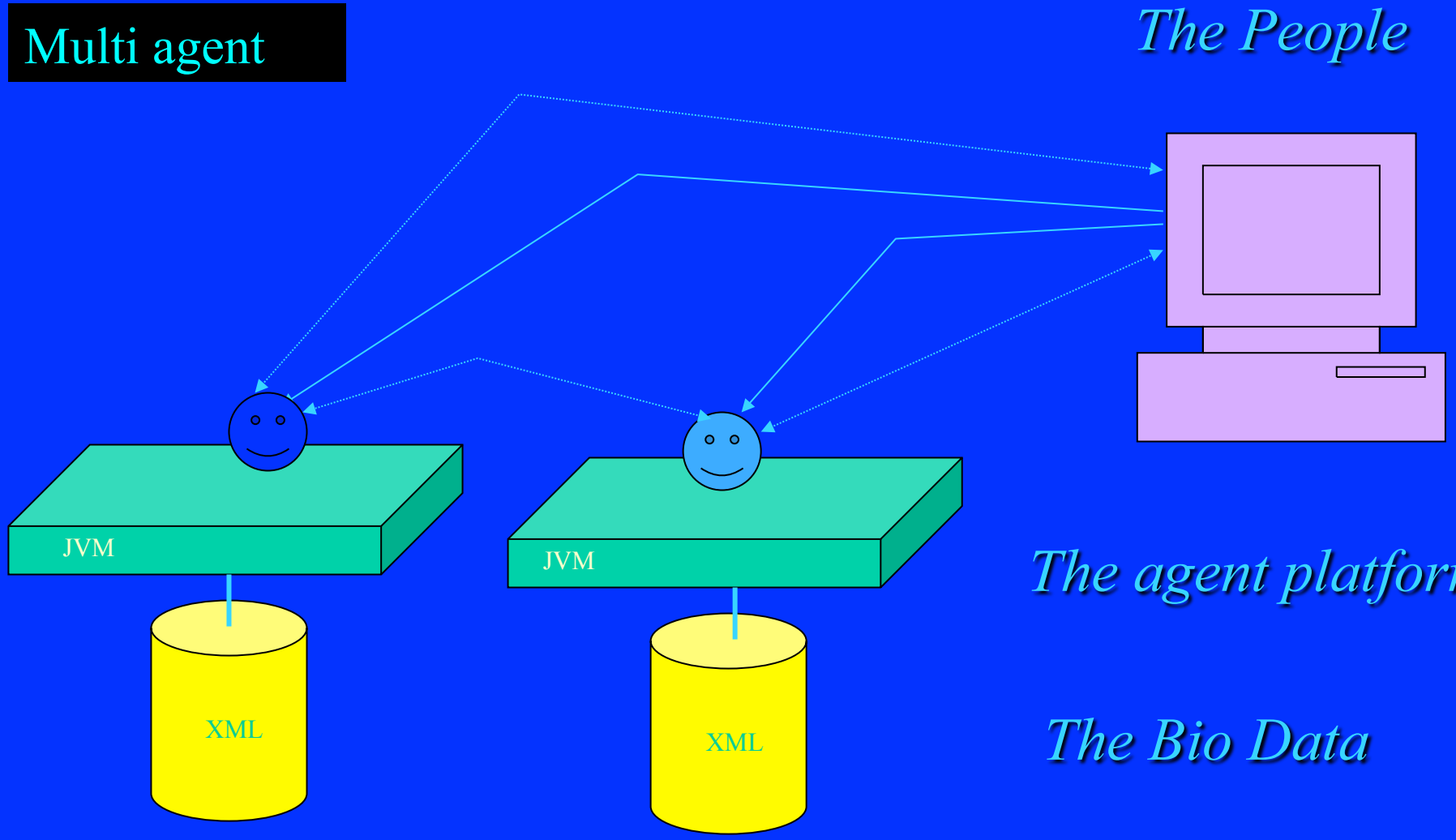


The agent platform

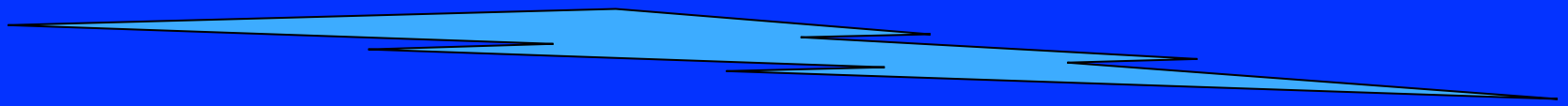
The Bio Data

How it works …

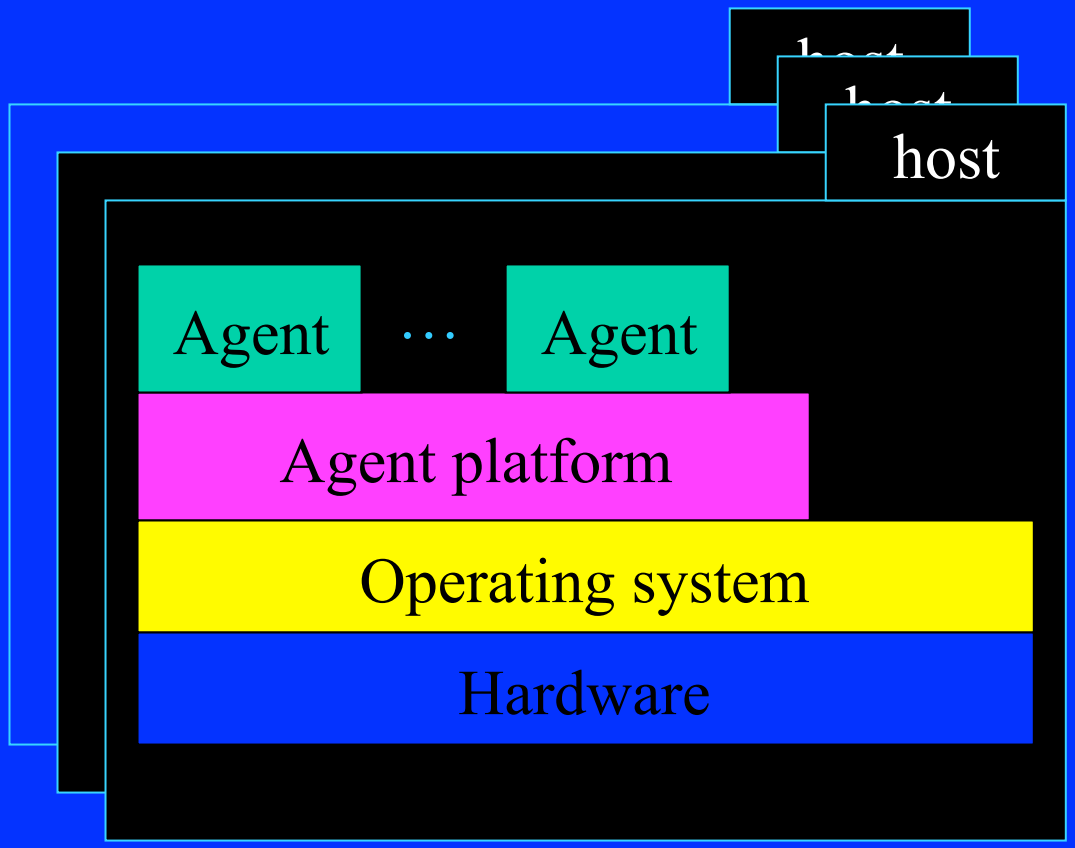
Multi agent



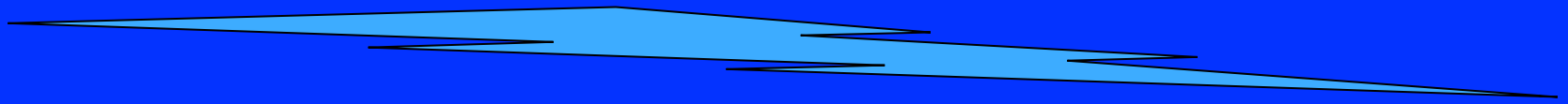
System’s architecture



System's architecture



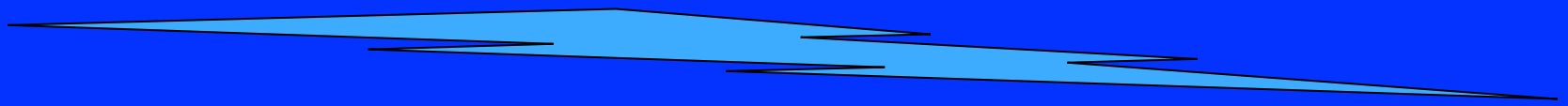
Agent model



Agent model

- Basic features
  - λ comunication, ability to exchange information with human customer or communicate and synchronize with others agents
  - λ memory, ability to freeze its status before to move
  - λ cloning, ability to instance a copy of itself
  - λ moving ability to move the code from one site to another
  - λ knowledge mng
- Application features
  - ability to believe, decide and enrich
  - λ Mission
  - λ Working Tools
  - λ Knowledge

Computational Analysis of Biological Data



Agent's Mission

- Bio data search
- Bio data integration
- Bio data clustering
- Bio data extraction
- Bio pattern recognition
- Bio knowledge discovering
- Bio data prediction
- ...

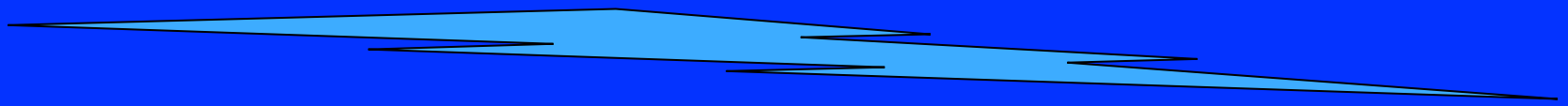
Agent's Working tools

- Optimization
  - λ Combinatorial algorithms
  - λ Heuristics algorithms
  - λ CLP: Constraints Logic Programming
  - λ ...
- Classification
  - λ Neural nets
  - λ Kohonen self-organizing map
  - λ ...
- Knowledge Discovering
  - λ Data mining
  - λ Multidimensional analysis
  - λ ...

Agent's Knowledge

- Basic knowledge (well-established)
  - λ dtd
- Extended knowledge
  - λ dtd ⟶ dtd', *new knowledge*
- Local knowledge
  - λ any, not in XML format

Application: analysis of gene expression



Data: Biological data related to an "organism"

- Experiment = set of inter-related hybridisations
- Hybridisation = collection of experimental data (spots). One spot for each ORF (Open Reading Frame)
- ORF = minimum bio data unit

Mission: analysis of hybridisation data

- Clustering by experiments
- Clustering by ORF

Tool:

- Kohonen self-organizing map

Basic Knowledge: MAML DTD

Exteded Knowledge: Kohonen map

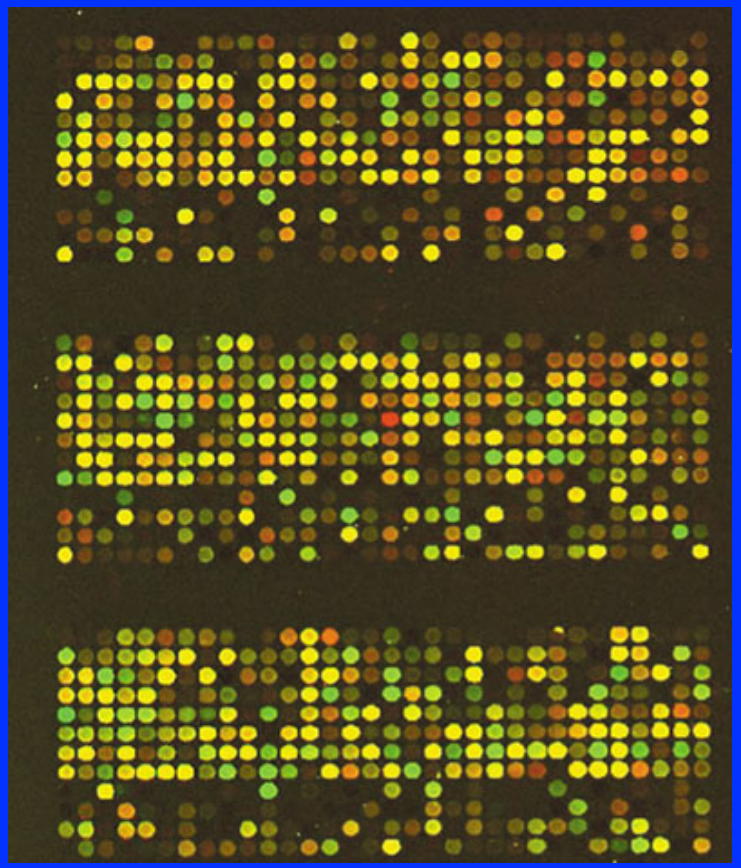
Microarray experiments

"…normally an experiment should include a set of hybridisations which are inter-related and performed in a limited period of time."

MIAME (Minimal Information About Microarray Experiments) document by MGED

(Microarray Gene Expression Database group, UK)

Hybridisation



- Each hybridisation is constituted by a collection of experimental data (spots) usually one spot for each ORF (Open Reading Frame).
- The intensity of each spot quantifies the expression of the related ORF under the chosen experimental conditions

MicroArray Markup Languages

- MAML proposed by the European Molecular Biology Lab (EMBL) and the European Bioinformatic Institute (EBI) and recently submitted to OMG (Object Management Group)
- GEML (proposed by a public-private coomunity, the GEML community [21]).
- BSML (Bioinformatic Sequence Markup Language) proposed by Visualgenomic, Inc. USA [20].

MAML DTD structure

- 1. Experimental design: the set of the hybridization experiments as a whole;
- 2. Array design: each array used and each element (spot) on the array;
- 3. Samples: samples used, the extract preparation and labeling;
- 4. Hybridizations: procedures and parameters;
- 5. Measurements: **images**, quantitation, specifications;
- 6. Controls: types, values, specifications.

Major goals pursued during the analysis of hybridization data

- data mining
- model-based/model-free
- functional classification
- clustering

Clustering

- Clustering using experiments euc. distance
  - λ (ORF “guilty-by-association”)
  - λ Present use: discover gene function
- Clustering using ORFs euc. distance
  - λ (transcriptional fingerprint)
  - λ Future use: diagnostic tool

Kohonen Algorithm

1. We define with $w_{ij}(t)$ the weights between the input neuron *ith* and the *jth* neuron in the map at time *t*. The weights initial values are random assigned in the [0,1] range.
2. Given an input $x_0(t)$, $x_1(t)$, ..$x_n(t)$, where $x_i(t)$ is the *ith* input
3. Calculate the distance d_i between input *i* and each output neuron *j*

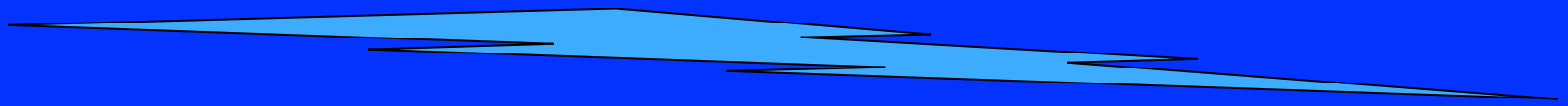
   $d_j^2 = \Sigma (x_i(t)-w_{ij}(t))^2$

4. Select neuron with minimum distance, *j**
5. Modify the weights of the input neuron *i* and *j** and its neighbours $N_i(j^*)$

   $w_{ij}(t+1) = w_{ij}(t) + \eta(t)(x_i(t)-w_{iJ}(t))$ for each *j* in $N_i(j^*)$ and $0 \le i \le n$

   $\eta(t)$ is a gain function $0 \le \eta(t) \le 1$
6. Cycle from step 2

Preliminary results



Database source

- 147 distinct hybridisation experiments
- 6053 ORFs

Agent's Platform

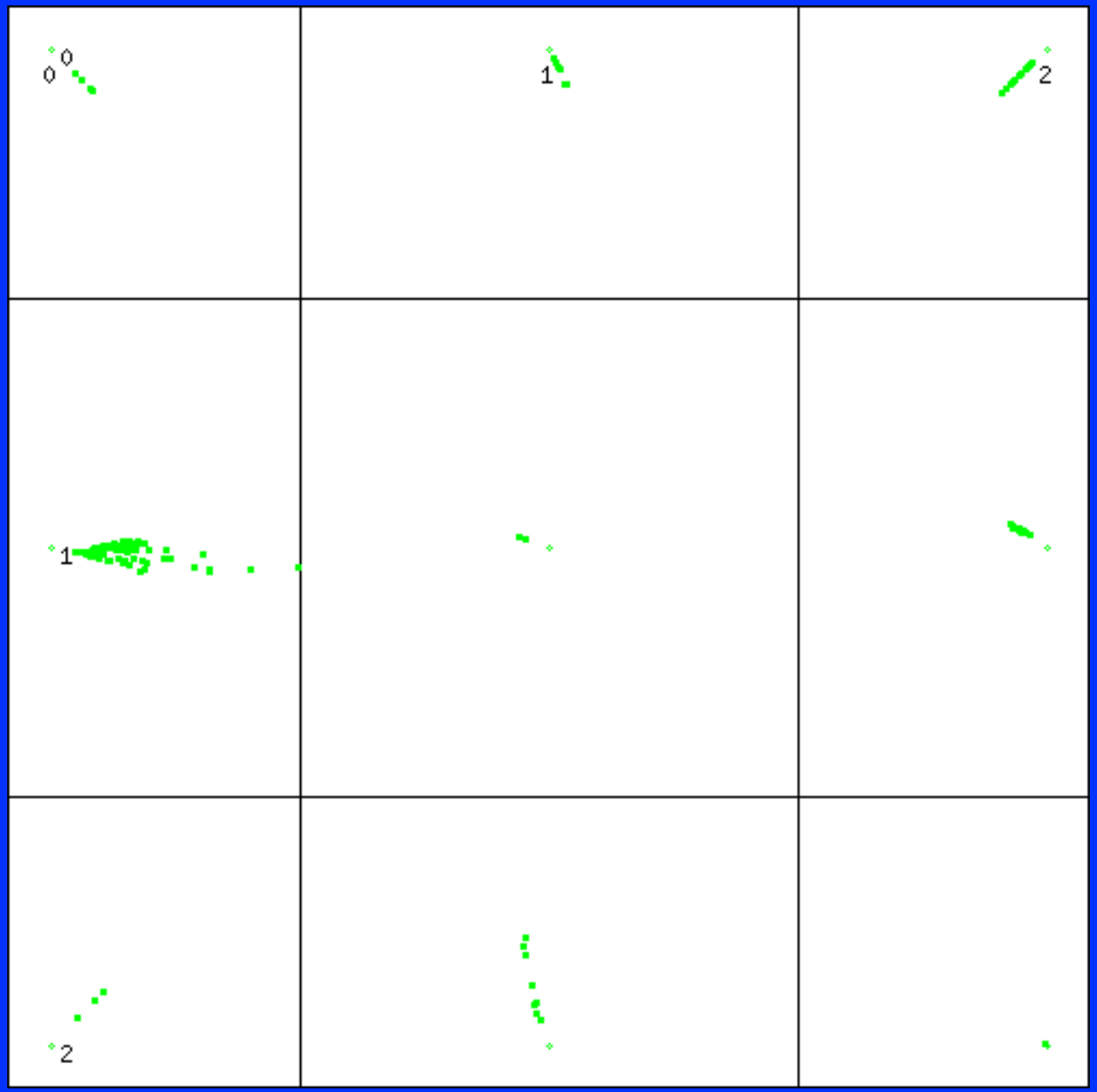
- *Macondo* [Ciancarini97]
- *MJada* for agents coordination and synchronization

Kohonen algorithm

- Completly implemented in Java
- 9 clusters

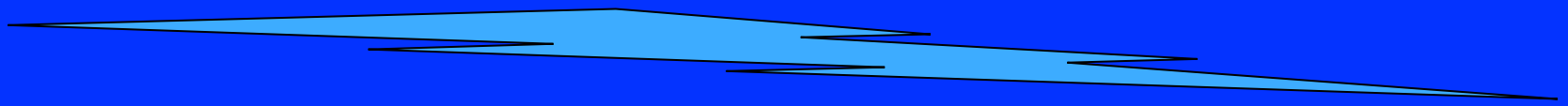
- The algorithm converges in 10000 cycles

The output



10000

On-going work



We are working on …

- Knowledge representation and mng
  - Model
  - Manipulation language
- IMABL
  - Declarative language for agent definition